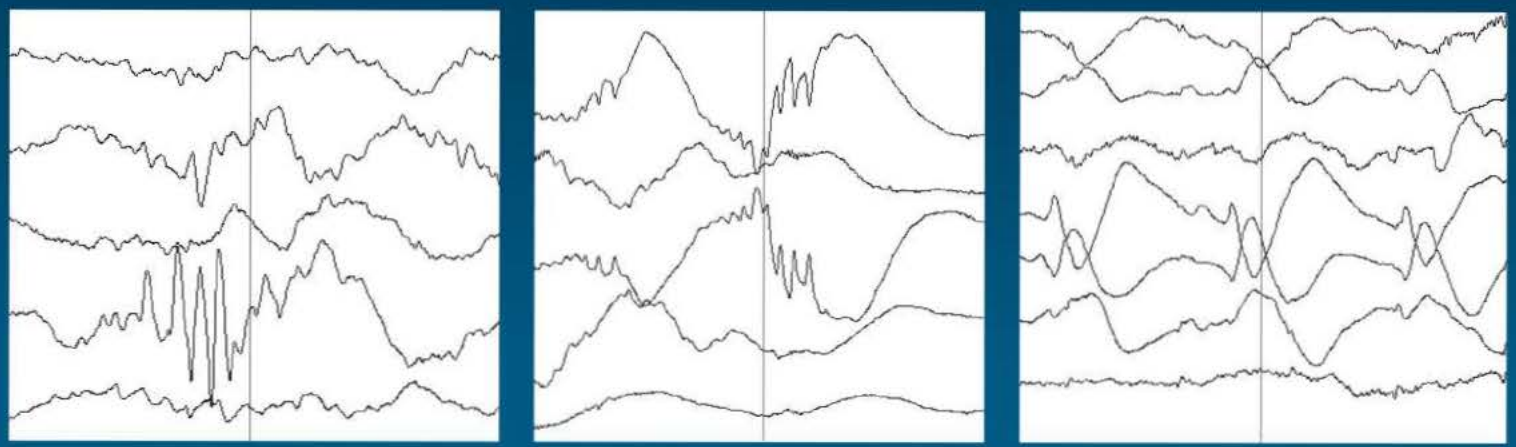
Atlas of Neonatal Electroencephalography



Eli M. Mizrahi • Richard A. Hrachovy

FOURTH EDITION

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ATLAS OF NEONATAL ELECTROENCEPHALOGRAPHY

ATLAS OF NEONATAL ELECTROENCEPHALOGRAPHY

Fourth Edition

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Preface

The practice of neonatal electroencephalography (EEG) combines clinical medicine and biomedical technology. It is based on the understanding of the general principles of EEG interpretation and age-dependent brain development unique to the neonatal period. However, this practice is limited by a gap in our knowledge between well-characterized features of some neonatal EEG findings and those that have yet to be clearly defined by clinical investigations. In considering these factors, we have written the *Atlas of Neonatal Electroencephalography*, *Fourth Edition*, to be a single-source reference concerning the practice of neonatal EEG based upon available information and current guidelines. Through text, tables, and samples of EEG recordings, we have tried to present a comprehensive view of the clinical practice of neonatal EEG for neurologists and clinical neurophysiologists; for trainees in neurology, clinical neurophysiology, and epilepsy; and for electroneurodiagnostic technologists.

As in the third edition of the *Atlas* (Mizrahi et al., 2004), this edition consists of chapters concerning the approach to visual analysis, techniques of recording, artifacts of noncerebral origin, age-dependent normal findings, patterns of uncertain diagnostic significance, age-dependent abnormal EEG findings, and seizures. Chapters consist of explanatory text, tables, a list of figures, and the sample EEGs themselves with their legends. For this new edition, the text and references have been updated and new EEG samples have been added to supplement those from the third edition.

We have presented information based upon the available referenced literature from a diverse group of clinical investigators representing several generations of neonatal neurophysiologists. In considering the aspects of neonatal EEG for which no studies are available and for which unresolved controversies persist, we have provided our own opinions. These have been formulated within our group and based upon our collective experience. Peter Kellaway, PhD, coauthored the third edition which went to press just prior to his death in 2003. He was integrally involved in the writing of that edition. As a pioneer in the development of neonatal and pediatric clinical neurophysiology his contributions to the third edition were invaluable. His ideas and concepts related to the practice of neonatal EEG that had been incorporated in the third edition and are carried forward in this current edition. In addition, over the years, we have written a number of articles, chapters, and reviews on neonatal and pediatric EEG and we have drawn from these works (Hrachovy et al., 1990; Kellaway, 2003; Kellaway and Hrachovy, 1982; Mizrahi, 1986; Mizrahi and Kellaway, 1998; Mizrahi et al., 2011).

The third edition of the *Atlas* was produced at a time when many laboratories were transitioning from analog recording devices to digital instrumentation. This is for the most part now complete with virtually all neonatal EEG recordings performed on digital equipment. Our figures still represent a

mixture of EEG samples derived both from analog-derived pen-and-ink and digital computer-based recordings. All of our recordings are presented as they were recorded in the course of clinical practice in our laboratory or at the bedside in the neonatal intensive unit. Unless otherwise indicated in figure legends, the recording parameters for all EEG channels on all samples are: sensitivity, 7 μV/mm; high-frequency filter, 70 Hz; low-frequency filter, 0.5 Hz (analog recordings), 1.0 Hz (digital recordings identified by the use of T7/T8 electrode designation rather than T3/T4); 60 Hz filter on; paper speed 30 mm/sec (analog recordings) and 10 sec/screen (digital recordings). Electrode placements for all recordings include: F1, F2, T3, T4, C3, C4, CZ, O1, O2 although additional electrodes may also have been placed. On some recordings T3 and T4 are designated as T7 and T8 consistent with recent guidelines by the American Clinical Neurophysiology Society which renamed these placements (ACNS, 2006a). They represent the same brain region. The abbreviations EKG and ECG are used interchangeably for electrocardiogram.

We realize the technical field of neonatal neurophysiology is rapidly expanding with the now almost routine use of bedside EEG-video monitoring and the increasing interest in the application of amplitude integrated EEG (aEEG) or cerebral function monitoring (CFM). We have provided some technical information concerning the methodology of EEG-video bedside monitoring but have not specifically addressed aEEG which is considered in detail elsewhere by expert investigators in that field (Boylan et al., 2013; Glass et al., 2013; Hellstrom-Wellas et al., 2003; Shah and Mathur, 2014; Shellhaas et al., 2007).

In presenting samples, we have emphasized specific components of the neonatal EEG. Our hope is that the fourth edition of the *Atlas of Neonatal Electroencephalography* will allow the neurophysiologist to recognize within a clinical recording the individual elements we have presented so as to determine their significance within the context of a complete recording. Throughout the *Atlas* we have emphasized the age-dependent nature of both normal and abnormal findings of the neonatal EEG and the need to correlate them with clinical data. The most valuable report of the findings of a neonatal EEG is one with clinical relevance that addresses the clinical questions raised by the referring practitioner.

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Acknowledgments

Two months after the completion of the third edition of the *Atlas of Neonatal Electroencephalography*, our coauthor, friend, mentor, and colleague Peter Kellaway, PhD, died at age 82. He was a pioneer in the development of neonatal and pediatric EEG. His academic career spanned 60 years—his first scientific paper appeared in 1943 and the third edition of the *Atlas*, which eventually appeared in 2004, was his last (Mizrahi and Pedley, 2004). We are grateful to have had the privilege to be trained by him and to have worked with him for more than 20 years until his death. We are particularly grateful to have been able to collaborate with him on that final project, which he saw to completion.

We also have been fortunate to collaborate with a number of valued colleagues at Baylor College of Medicine (BCM) and Texas Children's Hospital (TCH) in the development of our clinical, educational, and research programs in neurophysiology of the newborn. We are indebted to our colleagues in the Peter Kellaway Section of Neurophysiology, Department of Neurology, BCM, including James D. Frost, Jr, MD, Professor of Neurology and Neuroscience, BCM; Daniel G. Glaze, MD, Professor of Pediatrics and Neurology, BCM; Anne E. Anderson, MD, Associate Professor of Pediatrics and Neurology, BCM; and Merrill S. Wise, MD (Memphis, Tennessee).

We are also grateful to our group of electroneurodiagnostic technologists with expertise in neonatal recordings, including Nina Kagawa, R. EEG. T. (deceased 2007), Anita L. Thompson, R. EEG. T. (TCH), Kelvin L. Dillard, R. EEG. T. (TCH), and Lisa B. Rhodes, R. EEG. T., R. EP. T., CMIN (Baylor St. Luke's Medical Center, Houston, Texas). The electroneurodiagnostic technologists of TCH provide EEG services to neonates 24 hours per day, 7 days per week. We appreciate their dedication, patience, and expertise in generating the technically excellent recordings under difficult conditions and the compassionate care they provide to our young patients. We are also grateful to the pediatric neurologists, neonatologists, and nursing and other support staff of TCH who care for neonates. Finally, we are indebted to Katie Pierson, Administrative Assistant, Department of Neurology, BCM, for the editorial assistance she has provided in the development of both the previous and current editions of this *Atlas*.

In addition, we acknowledge the authors of the first and second editions of this series who pioneered and developed the neonatal EEG atlas, Janet E. Stockard-Pope, Sarah S. Werner, MD, and Reginald G. Bickford, MB B Chir (Stockard-Pope et al., 1992; Werner et al., 1977).

We gratefully acknowledge the National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), which supported the Clinical Research Center for Neonatal Seizures (NS-1-12316; E.M.M., P.I.). In addition, research in the Peter Kellaway Section of Neurophysiology, Department of Neurology is supported in part by the Peter Kellaway Endowment for Research of BCM. Finally, we are indebted to TCH for the support provided in the development of clinical neurophysiology services, research in neonatal EEG, and commitment to the care of newborn infants.

CHAPTER 1

Approach to Visual Analysis and Interpretation

The basic principles of visual analysis and interpretation of the electroencephalogram (EEG) that apply to older patients (Kellaway, 2003) also generally apply to neonates, although with some additional special considerations. For example, because of the rapid rate of cerebral development in the neonatal period, the age-dependent features of the EEG become critically important. The interpretation of the neonatal EEG requires the recognition of EEG changes from conceptional ages (CAs) less than 28 weeks through 44 weeks. In addition, types of abnormalities that are age-dependent must also be identified. Further, because of the special clinical problems of neonates, it is critical to understand how specific etiological factors may affect cerebral function and, in turn, the neonatal EEG.

Nearly 50 years ago it was pointed out that the characteristics of the EEG known to be normal and, to a lesser degree, abnormal in neonates had not been established (Kellaway and Crawley, 1964); in 2015, the situation has only modestly improved. One problem is that an assumption of normality cannot be made in a newborn with the same degree of confidence as it can in older children. This is related to the brevity of the period of life available for study, the limitations of the neurological examination, and the limitations of longitudinal studies that would consider the impact of intercurrent disease on long-term development. Traditionally, in studies of neonatal EEG, infants have been considered normal if they had no abnormal neurological signs at birth and were clinically normal at the time of discharge from the hospital. Some manifestations of cerebral dysfunction may not become clinically evident until a certain level of brain maturation has been achieved. In addition, to date, systematic, long-term serial studies that correlate neonatal EEG with neurological, psychological, and behavioral development from birth to adolescence have not been carried out. As a consequence of these limitations, the significance of certain specific features of the EEG has not been established.

In current practice, it is generally assumed that, without intercurrent injury, the infant will demonstrate developmental EEG features based upon either intrauterine or extrauterine determined CA (Selton et al., 2010). Recent data suggest that preterm infants, when reaching term, may have less mature EEG patterns than matched controls (Nunes et al., 2014). In addition, more detailed longitudinal studies have begun to reexamine and verify the normal features of the neonatal EEG (Crippa et al., 2007; Dos Santos et al., 2014; Korotchikova et al., 2009; Vecchierini et al., 2003).

Despite these limitations, the imperatives of clinical practice require a clear presentation of the current knowledge of neonatal EEG. The data presented in this atlas reflect our experience in the study of normal and abnormal neonates and, importantly, the work of other investigators (Blume and Dreyfus, 1982; Clancy et al., 1993; Dreyfus-Brisac, 1957, 1959, 1962, 1964, 1968, 1970, 1978; Dreyfus-Brisac and Blanc, 1956; Dreyfus-Brisac and Monod, 1970; Dreyfus-Brisac et al., 1957, 1961, 1962; Ellingson, 1958, 1979; Engel and Butler, 1963; Lombroso, 1979, 1982, 1985; Monod and Pajot, 1965; Monod et al., 1960, 1972; Sainte-Anne-Dargassies et al., 1953; Tharp et al., 1981; Torres and Anderson, 1985; Torres and Blaw, 1968; Watanabe and Iwase, 1972; Watanabe et al., 1974). In this regard, we owe a large debt to the pioneering French group led by Dreyfus-Brisac. The group's early studies of the EEGs of premature infants were conducted in a rich institutional environment that was virtually unique in those days. They provided the basic insights that facilitated consistent progress in the development of knowledge and rational interpretation of the EEG of the newborn.

TERMINOLOGY RELATED TO AGE-DEPENDENT DEVELOPMENTAL FEATURES

Traditionally, age-dependent developmental features of the neonatal EEG have been defined in terms of CA. In 2004, the American Academy of Pediatrics (AAP) issued a policy statement, developed by its Committee of Fetus and Newborn, recommending standardization of terminology to describe age during the perinatal period. The AAP recommended the use of the post-menstrual age (PMA) rather than CA (Committee on Fetus and Newborn, 2004). The PMA is calculated as gestational age measured from the time of the last menstrual period plus the chronological age. The Committee recommended against the use of the term CA. The Committee also recommended that in publications reporting fetal and neonatal outcomes, methods should be clearly defined to determine gestational age. The use of the term CA is well-engrained in the historical and current literature related to neonatal EEG and we will continue to use this terminology in this atlas. Thus, gestational age is in the calculation of the use of CA, the last menstrual period occurs approximately 2 weeks before conception.

THE PROCESS OF VISUAL ANALYSIS

In the interpretation of the EEG of children and adults, we believe that the only data that should be considered before visual analysis is initiated are the age and the state of consciousness of the patient (Kellaway, 2003). When interpreting EEGs of neonates, the first of these should not be considered or known, because the determination of the EEG CA is a critical part of the analysis and assessment of the recording. It is recognized that the determination of the state of consciousness of the neonate may be difficult to determine, but as will be shown later, it may have impact on the eventual interpretation of the recording.

Analysis of the neonatal EEG is initially directed toward the determination of CA based upon detection and the recognition of the various developmental features occurring in the record (see Chapter 4). If the EEG lacks recognized developmental features that would permit the determination of CA, then this, in itself, may be evidence of brain dysfunction. Developmental EEG features may suggest a specific CA, but there may be discrepancies between the clinically determined CA and the EEG-derived CA, referred to as *external dyschronism*. This may simply arise from a miscalculation of the clinically determined age, and is most likely if the EEG is normal in all other respects. The developmental characteristics of the EEG in deep non-rapid eye movement (NREM) sleep may be more immature than those of the EEG when awake and in light sleep; referred to as *internal dyschronism*. In this instance, the most immature features of the deep NREM sleep findings reflect the age at or before which a cerebral insult may have occurred.

The final step in the process of analysis is the detection and characterization of any abnormal features that may be present. These features may also be age-dependent, are described in Chapters 5 to 7, and include characterization of background activity and focal features.

As in older children and adults, visual analysis of the EEG of newborns should be an orderly process, involving a series of logical steps that result in the *technical analysis* and upon which *interpretation* is based. Only then should a correlation be made with the clinical history and findings to derive a *clinical impression*. **Figure 1.1** summarizes the steps of this intellectual process.

THE CLINICAL IMPRESSION

The neonatal EEG can be a powerful tool when applied to specific clinical questions (**Table 1.1**). However, the usefulness of the EEG in these situations will depend upon the scope and quality of the information provided by the referring physician and also upon the clinical neurophysiologist's understanding of the neurological disorders of newborns.

What Is the CA?

The CA-dependent features of the neonatal EEG are the character of the background activity, the presence of wake–sleep stages, specific waveforms and patterns (collectively referred to as *graphoelements*) and reactivity (see Chapter 4). Recognition of these features allows the clinical neurophysiologist to determine the CA of an infant usually within a 2-week epoch. There may be clinical circumstances in which the CA of the infant is unknown, indeterminate, or based upon inconsistent data from maternal history, infant physical examination, or prenatal head ultrasound. However, determination of an accurate EEG-derived CA may add to the understanding of ongoing clinical problems and assessment of the potential risk of future concerns.

Is There Evidence of Focal Brain Dysfunction?

As in older children and adults, the EEG in neonates may demonstrate the presence of a consistent focal brain abnormality. Findings such as persistent voltage asymmetries, focal slow activity, and recurrent and persistent sharp waves—either in isolation or in combination—may indicate focal intracranial abnormalities such as subdural fluid effusion, subarachnoid hemorrhage,

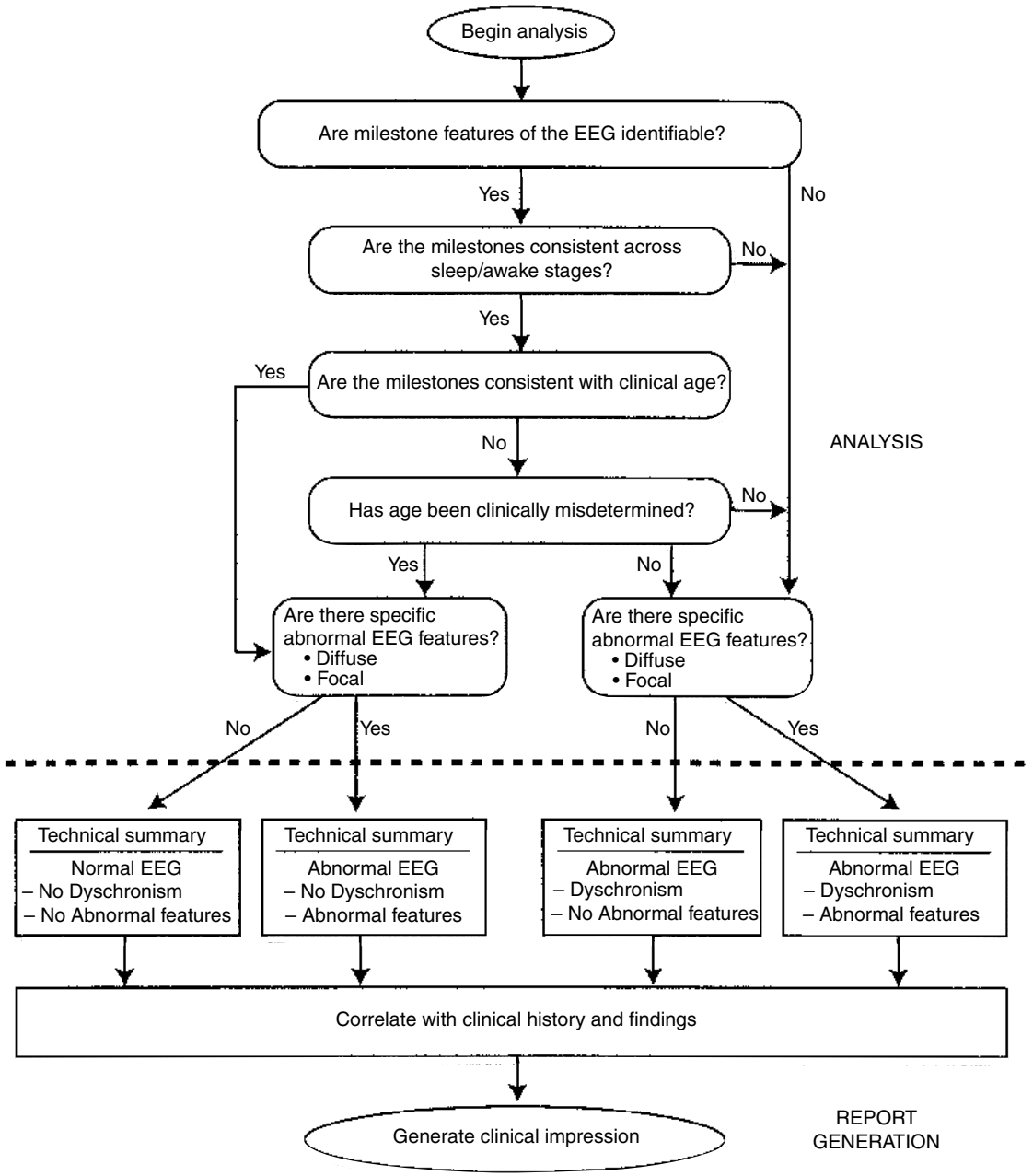

Figure 1.1 Flow diagram showing the process of visual analysis and interpretation of the neonatal EEG.

Table 1.1 Clinical Questions That Can Be Addressed by the Neonatal EEG

- What is the conceptional age?
- Is there evidence of focal brain dysfunction?
- Is there evidence of diffuse brain dysfunction?
- When did the brain insult occur?
- Are there clinical or electrical seizures?
- What is the neurological prognosis?
- Is there an indication that a specific disease entity is present?

intracranial hemorrhage, cystic or atrophic lesions, cortical infarction, cerebral malformation, or other focal processes.

Sharp waves may suggest brain injury that is either *focal* when sharp waves are persistent and unifocal, or *diffuse* when sharp waves are multifocal (see Chapters 5 and 6). However, focal sharp waves are rarely indicative of epileptogenicity in the newborn (see Chapter 7) (Mizrahi and Kellaway, 1998). Positive rolandic sharp (PRS) waves were initially associated with the presence of intraventricular hemorrhage (IVH) in the premature infant (Dreyfus-Brisac and Monod, 1964). Subsequently PRS waves have been shown to be associated with periventricular leukomalacia, a condition that may be in part a consequence of various disorders including IVH (Clancy and Tharp, 1984; Novotny et al., 1987). Focal sharp waves that recur in a periodic fashion have been associated with herpes simplex virus encephalitis (Mikati et al., 1990; Mizrahi and Tharp, 1982). It should be noted that the significance of some types of sharp waves in the neonatal EEG are unknown and are discussed further in Chapter 5.

Is There Evidence of Diffuse Brain Dysfunction?

The neonatal EEG may indicate the presence and degree of diffuse brain dysfunction. While it may provide evidence of an encephalopathy and its severity, the EEG is less likely to provide information concerning etiology. Thus, similar findings of abnormal background activity may be present in infants with hypoxic-ischemic encephalopathy, central nervous system (CNS) infections, bilateral cerebral hemorrhage or infarctions, some metabolic disturbances, genetic syndromes, and other etiologic factors that may cause diffuse CNS injury.

The characterization of abnormalities of the background activity that describe the continuum of diffuse dysfunction are, from the least to the most severe, multifocal sharp wave, and episodes of generalized voltage attenuation, depressed and undifferentiated, suppression-burst and isoelectric (see Chapter 6). The timing of these findings in relationship to injury may suggest both severity of the encephalopathy and its prognosis, since some abnormal findings obtained in the acute period following injury may be only transient. Additional findings that suggest diffuse brain dysfunction are those characterized by internal dyschronism.

When Did the Brain Insult Occur?

No formal studies link EEG findings with the determination of the time of occurrence of diffuse brain injury. However, a number of assumptions have been made in the application of EEG in relationship to this clinical question. As discussed earlier, internal dyschronism is when the developmental features of the EEG in deep NREM sleep are more immature than in wakefulness and light sleep and may suggest cerebral dysfunction. The CA derived from the features in deep sleep may indicate that an insult occurred at or before the developmental age associated with those specific features.

Are There Clinical or Electrical Seizures?

The clinical problem of neonatal seizures is discussed in Chapter 7 and, in more detail, elsewhere (Chapman et al., 2015; Clancy et al., 2013; Mizrahi and Kellaway, 1998; Mizrahi and Pressler, 2015). Recording seizures is dependent upon the duration of the EEG recording and its timing. Seizures may be classified according to the temporal relationship of clinical and electroencephalographic events. Electroclinical seizures are those in which clinical and EEG seizure activity overlap in time, typically with close correlation of limb, body or facial movements to electrical discharges. Electrical only seizures are those that occur without clinical events. Clinical only seizures are those without any EEG correlate.

Interictal findings, such as the character of the background, may be helpful in assessing the degree and distribution of CNS dysfunction and may even suggest the degree of risk of seizure occurrence (Laroia et al., 1998). However, interictal focal sharp waves are not reliable markers of potential epileptogenesis. Focal sharp waves or even spikes do not always have the same implications in the neonate as they do in older children or adults and therefore may not be considered epileptiform.

What Is the Prognosis?

Some features of the EEG that indicate focal or diffuse injury may also suggest the long-term neurological prognosis. For example, the frequency of occurrence of PRS waves may predict the occurrence of neurological sequelae (Blume and Monod, 1982); and a severely abnormal background activity may also suggest a poor prognosis. However, the overriding factor in the use of neonatal EEG in determination of prognosis is the evolution of findings over time in sequential studies. A single normal EEG recorded at or near the time

of suspected injury usually predicts a good outcome. An initial EEG with an abnormal background, even when severely abnormal, may, over time, evolve to less abnormal or even a normal recording depending upon the nature of the brain insult. The rate of resolution, if any, will be more predictive of outcome than a single EEG at a single given point in time.

Is There an Indication That a Specific Disease Entity Is Present?

In general, it is unusual for the neonatal EEG to provide data that will identify specific disease entities. There are only a few patterns that are diagnostic. PRS waves traditionally have been associated with the presence of IVH, but now are more consistently associated with periventricular leukomalacia (Clancy and Tharp, 1984). Herpes simplex virus encephalitis has been associated with the finding of periodic lateralized epileptiform discharges (Mizrahi and Tharp, 1982), although this finding may be also found in other conditions (Hrachovy et al., 1990). The condition of holoprosencephaly is associated with a specific pattern of rapidly changing background activity (DeMyer and White, 1964). A pattern of periodic hypsarrhythmia in term infants has been associated with nonketotic hyperglycinemia, other inborn errors of metabolism, and an emerging group of genetically determined encephalopathies (Aicardi, 1985; Mizrahi and Milh, 2012; Ohtahara, 1978). These patterns are discussed in Chapter 6.

CHAPTER 2

Techniques of Recording

GENERAL PRINCIPLES

The general principles of recording the electroencephalogram (EEG) in older children and adults apply to the recording of the EEG in neonates with some important additions and exceptions. Guidelines for the recording of the neonatal EEG have been established and recently updated by the American Clinical Neurophysiology Society (ACNS, 1986, 2006b) and the International Federation of Clinical Neurophysiology (De Weerd et al., 1999). In addition ACNS guidelines have been proposed for continuous EEG monitoring in neonates and standardized terminology for these studies (Tsuchida et al., 2013).

Personnel

Critical to the recording of neonatal EEG is a well-trained staff of electroneurodiagnostic technologists (ENDTs) with expertise in the recording of newborn and young infants. Such technologists provide the expert interface between the patient, the direct care givers, and the interpreting clinical neurophysiologist by ensuring technical excellence; a clinical understanding of neonatal care; detailed observation of normal and abnormal infant behaviors; a good working relationship with nursing staff; and a compassionate and caring relationship with parents who may be at the bedside during recording. Technologists require specialized training to produce clinically relevant records.

Clinical neurophysiologists with expertise in the interpretation of neonatal EEG are also essential. The neurophysiologist should be familiar with the clinical problems that neonates may encounter to provide individualized and relevant interpretations and clinical correlations.

It is most helpful for neonatal EEG services to be available 24 hours per day, 7 days per week since the most frequent reasons for referral are for suspicion of onset or ongoing clinical seizures and acute alteration of mental status. In order for the EEG to be most valuable in the assessment of these infants, it best be available around-the-clock with specialized instrumentation, ENDTs and clinical neurophysiologists.

Biomedical engineering, information technology, and other technical support staff familiar with recording software, hardware, and network applications are essential members of the neonatal EEG team.

DATA COLLECTION

The findings of the neonatal EEG are most valuable when considered in relationship to an individual patient's history and clinical findings. Initially, the ENDT obtains basic information about each neonate to be recorded. This information typically collected in the Texas Children's Hospital (TCH) neurophysiology laboratory is listed in **Table 2.1** and includes standard demographic data, description of the recording environment, documentation of reason for referral, details of the medical history, a list and timing of medications, and the specifics of the infant's general medical and neurological condition. This information may be obtained from the infant's referring physician, parents, and medical record. Thus, the technologist must be trained to be familiar with the medical issues of neonates. To aid in data collection, a

Additional contributors to this chapter: Lisa B. Rhodes, R.EEG.T., R.EP.T., C.N.I.M., Baylor St. Luke's Medical Center, Houston, TX, and Anita L. Thompson, R.EEG.T., Texas Children's Hospital, Houston, TX.

Table 2.1 Data Collection for Recording of the Neonatal EEG

1. Patient demographic information
   a. Name
   b. Date of birth (chronologic age)
   c. Stated estimated gestational age at birth
   d. Birthweight
2. Recording environment
   a. Location
      i. Hospital nursery
         1. Routine
         2. Special care units
      ii. In laboratory
   b. Crib type
      i. Open bassinette
      ii. Isolette
      iii. Infant warmer
   c. Additional instrumentation
      i. Monitors
      ii. Ventilator
      iii. Phototherapy
      iv. Extracorporeal membrane oxygenation
3. Reason for referral
   a. Altered mental status
   b. Determination of conceptional age
   c. Identification of diffuse cerebral disturbance
   d. Identification of focal cerebral lesion
   e. Suspected seizures
      i. Description of suspected clinical event
      ii. Timing and duration of events
   f. Other
4. Medical history
   a. Prenatal
      i. Maternal history
      ii. Pregnancy history
   b. Perinatal
      i. Route of delivery
      ii. Apgar score
      iii. Requirements for delivery room resuscitation
   c. Postnatal
      i. Hospital course since delivery
      ii. History at home after initial discharge
5. Medications
   a. Drug
      i. Sedation
      ii. Antiepileptic drugs
      iii. Paralytic agents
      iv. Other
   b. Dose
   c. Timing
      i. Date
      ii. Hours
      iii. Routine schedule
   d. Route of administration
   e. Recipient
      i. Neonate
      ii. Maternal (with potential neonatal effect)
6. General medical condition
   a. Medical treatments
      i. Limb restraints
      ii. Intravascular lines
      iii. Intubation
      iv. Gastric tube access
      v. Other
   b. Physical condition
      i. Body position
      ii. Recent surgical wounds
      iii. Healed scars
      iv. Scalp swelling
      v. Ventriculo-peritoneal shunt
   c. Degree of infant comfort
      i. Comfortable, without distress
      ii. Irritable when handled, but consolable
      iii. Inconsolable
   d. Apparent mental status
      i. Awake and alert
      ii. Difficult to arouse
      iii. Nonresponsive
   e. Feeding
      i. Type
      ii. Route (oral, tube)
      iii. Schedule
      iv. Time of late feeding

well-designed data collection form, which can be tailored for use in each neurophysiology laboratory, is helpful and eventually becomes part of the infant's laboratory and hospital medical record.

INFANT PREPARATION

The recording of the neonatal EEG may be routine within the context of special care units where parents become familiar with the many medical procedures performed on their infants. However, it may be a unique experience for the infant and parents in the outpatient setting. In either circumstance, the ENDT attempts to put the family at ease by explaining the procedure and answering any questions and concerns.

The clinical state of infants may vary: They may be content and comfortable, difficult to console, irritable, excessively sleepy or lethargic, or comatose. The technologist must consider the state of each infant and determine the best method to make the infant as comfortable as possible to obtain a complete recording. This may require having the infant fed, having diapers changed, adjusting room temperature and, often, prolonging the recording until the infant becomes comforted. The purpose of these efforts is to facilitate a recording of spontaneous sleep cycles as well as with the infant awake.

ELECTRODE PLACEMENT

The International 10-20 System of Electrode Placement (Jasper, 1958), has been modified for recording neonates (**Figure 2.1**) (ACNS, 2006b; Kellaway and Crawley, 1964; Tekgul et al., 2005). This is to accommodate the neonate's immature frontal lobes that do not extend as anteriorly relative to the skull compared to older children and adults. Typically, nine scalp positions are used (F1, F2, C3, C4, CZ, T3, T4, O1, O2) although others may be added. The ACNS modified terminology replacing T3/T4 with T7/T8 and T5/T6 with P7/P8 (ACNS, 2006a). In addition, electrodes are also placed at A1 and A2 and a ground electrode is placed either at midforehead or on a mastoid region. Since digital recordings are fundamentally referential, an additional reference electrode position may be needed (typically noncephalic), although some instruments provide a so-called "internal" reference. The F1 and F2 electrode positions are 20% of the inion-nasion distance above the nasion and 10% of the circumferential measurement from the midline. For neonates, placement of all of the standard electrodes of the International System would result in such close spacing on the infant's scalp that many electrodes would record overlapping, and thus redundant, electrical fields. The optimal number of electrodes has not been determined, but the clinical experience in our laboratories has shown that the nine cephalic

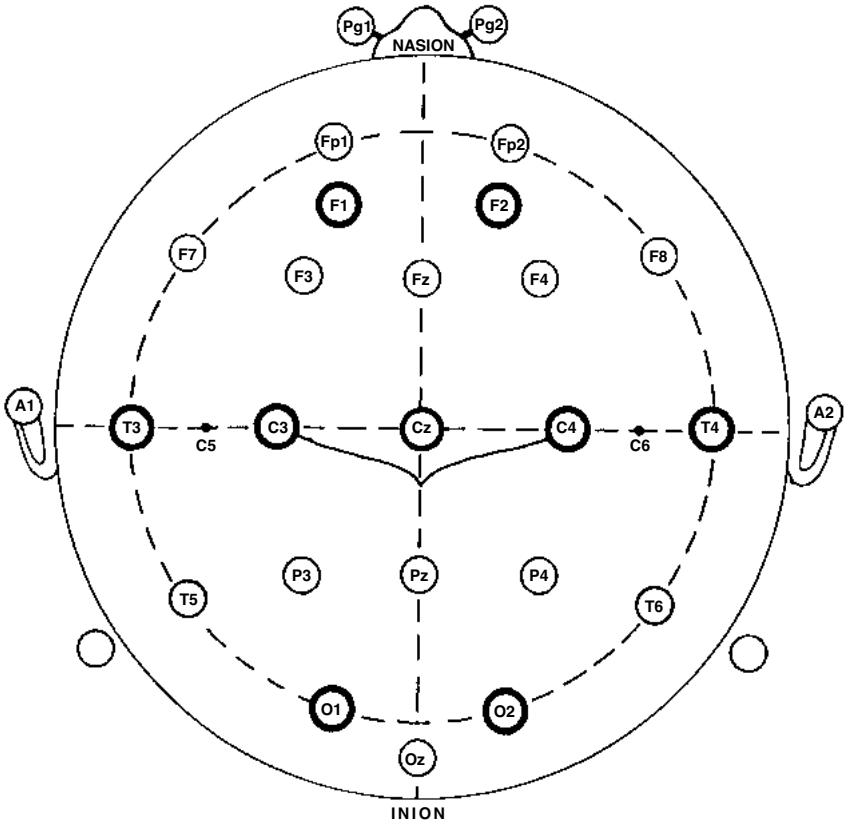

Figure 2.1 Electrode placement modified for neonatal EEG superimposed on the 10–20 electrode placement system.

positions designated previously are sufficient to characterize the normal neonatal EEG and to detect, localize, and characterize major abnormalities.

After head measurement, the scalp is prepared with slight abrasion at each electrode site with a mild abrasive gel utilizing the soft end of a cotton applicator. This may cause slight erythema at the site, but this is a temporary effect. Conductive paste is used to secure the electrodes. A ball of cotton is placed over each electrode and the electrode array is finally secured with paper tape. Paste can be used successfully for even lengthy recordings when applied and attended to by experienced ENDTs. Collodion is typically not utilized for routine neonatal EEG for a number of reasons. The environment in which collodion is applied must be well ventilated since it is flammable and may be toxic to the lungs. This is a particular problem for infants in special

care units who may be in confined areas such as isolettes that may concentrate fumes and for those infants with already compromised pulmonary function.

POLYGRAPHIC PARAMETERS

Polygraphic measures are integral to the recording of the EEG to assist in characterizing sleep states, eye movements, muscle contractions, cardiac rhythms, and respiratory patterns (ACNS, 1986, 2006b; DeWeerd et al., 1999; Hanley, 1981; Kagawa, 1973; Mizrahi, 1994). The same procedures are followed for electrode application as described previously for scalp electrodes. The basic polygraphic parameters are as follows.

Electrooculogram

The electrooculogram (EOG) is recorded to detect and characterize eye movements. This assists in staging sleep and in the determination of the origin of some electrical potentials recorded in anterior cephalic electrodes that may have been generated by eye movement. For bipolar EOG recordings, one electrode is placed below and lateral to the outer canthus of one eye and one above and slightly lateral to the nasion. This positioning will capture both horizontal and vertical eye movements.

Electromyogram

The submental electromyogram (EMG) is recorded to assist in sleep staging and also to characterize some oral-lingual-pharyngeal muscle movements that may also contaminate the EEG. The EMG is recorded with electrodes placed bilaterally and symmetrically, immediately under the jaw. When movements recur in limbs, EMG may be recorded in order to determine the precise relationship of such movements to any change in the EEG.

Electrocardiogram

The electrocardiogram (ECG or EKG) is monitored to assess heart rate and rhythm. One electrode is placed over the midline chest and referenced to the right ear for a single channel recording of ECG. It may also be utilized to identify waveforms recorded from EEG electrodes that might have been generated by ECG.

Respiration

Respiration is recorded to assist in sleep staging, to characterize various types of apnea, and to assist in differentiating respiratory or body movements from EEG. The methods used for the recording of respiration may be complex. The most complete method of characterizing respiration is by measurement of abdominal movement (typically with a strain gauge or pneumograph adapted to abdominal placement), thoracic movement (with a strain gauge, bipolar electrodes, or pneumograph adapted to thoracic placement), air flow at the nares or mouth (with a thermocouple device or other flow measurement devices), end-expiratory CO_2 and O_2 saturation with a pulse oximeter.

Specialized Polygraphic Measures

There are a number of other parameters that can be measured time-locked to EEG. These are most often used in research protocols or special clinical circumstances. The physiologic measure of significant interest includes systemic blood pressure and blood oxygen saturation. There are instrumentation-specific interfaces to measure these parameters. Alternatively changes in these measures may be noted by the ENDT as they occur.

MONTAGE SELECTION

Important strategies in the recording of the neonatal EEG are the documentation of wake/sleep cycles, the characterization of reactivity of the record to stimulation and identification of age-dependent *graphoelements* (see Chapter 4). These are best achieved in a sustained recording using a single, bipolar montage with broad coverage over the scalp. In the recording of older children and adults, localization of focal abnormalities often requires the use of several montages; however, because of the range of abnormalities in neonates and the overriding need to characterize state changes over time, multiple montages are not used. A typical montage, with adequate coverage over the scalp, including the required channels with a Cz electrode placement, is given in **Table 2.2** and is similar to those listed in ACNS guidelines (ACNS, 2006). Digital recording of the neonatal EEG provides the opportunity to examine various waveforms with different montages after recordings are complete (Levy et al., 1998).

INSTRUMENT SETTINGS

Instrument settings used at the onset of recording are listed in **Table 2.3**. The filter settings and sensitivity of all the EEG channels should be the same. In addition, the filter settings and sensitivity for EOG should be the same as the EEG channels to allow accurate comparison of waveforms to differentiate

Table 2.2 Sample Neonatal Montage Selection

Channel 1	F1–C3
Channel 2	F2–C4
Channel 3	C3–O1
Channel 4	C4–O2
Channel 5	T3/T7–C3
Channel 6	C3–Cz
Channel 7	Cz–C4
Channel 8	C4–T4/T8
Channel 9	F1–T3/T7
Channel 10	F2–T4/T8
Channel 11	T3/T7–O1
Channel 12	T4/T8–O2
Channel 13	EOG
Channel 14	EMG
Channel 15	ECG
Channel 16	Resp

Table 2.3 Initial Instrument Settings

EEG channels				
Sensitivity	7 μV/mm			
Low-frequency filter	0.5 Hz			
High-frequency filter	70 Hz			
Notch filter (60 Hz, 50 Hz)	Off			
Display time				
Paper speed	30 mm/sec			
Screen display	10 sec/screen			
Polygraphic channels				
	EOG*	EMG**	Respir.**	ECG**
Sensitivity	7 μV/mm	7 μV/mm	7 μV/mm	300 μV/mm
Low-frequency filter	0.5 Hz	5 Hz	0.5 Hz	0.5 Hz
High-frequency filter	70 Hz	70 Hz	70 Hz	70 Hz
Notch filter (60 Hz, 50 Hz)	Off	Off	Off	Off

*EOG settings remain the same as EEG settings for comparison of simultaneously recorded waveforms.

**EMG, Respir. (pneumograph), and ECG settings may be adjusted to optimize display.

cerebral activity from that of ocular origin. Traditionally, paper speed was set at 30 mm/sec when analog, pen-and-ink recordings were made. Now this parameter is set at 10 sec/screen or "page" for digital recordings. These so-called "paper speed" settings are used in many laboratories in the United States and are used in this atlas. However, several laboratories, particularly those with ties to the French school of recording, use a slow speed: 15 mm/sec or 20 sec/screen or "page" (Plouin et al., 2005).

VIDEO

There is considerable interest in time-synchronized EEG-video monitoring of neonates (Boylan et al., 2002; Bye et al., 1997; Clancy, 1996; Mizrahi and Kellaway, 1987; Scher, 1997). While this technique was originally used in a research setting, at many centers it has become routine. At the outset, it may seem as if the addition of video to the recording of neonatal EEG would be relatively easy particularly with light-weight, low-light, digital video cameras added to portable digital EEGs. However, many of the difficulties that were present during the development of these techniques still persist.

Nursery Environment

The most challenging aspect of neonatal EEG-video monitoring is effective integration of recording efforts with the essential activities of the nursery. Instrumentation, camera mount, electrode cables, and junction box must all be placed so as not to interfere with the ongoing care of the neonate. A good working relationship between the ENDT and the nursing staff is essential for optimal recording. It is also important to keep the video image as free as possible from personnel and instruments that block the camera view. In addition, when the infant is experiencing sudden clinical events suspected of seizure activity, it is essential for personnel not to interfere with the infant if clinically safe and to allow the recording of the entire seizure. The ambient temperature of the recording environment should be controlled as best as is possible. From a clinical need, it is important to keep the infant warm and covered. However, for infants studied with suspected seizures, it is essential that the infants remain uncovered with all limbs in full view of the camera. These concerns are best addressed with nursing staff at the onset of the recording session at the bedside and with parents at the bedside or in the neurophysiology laboratory.

Infant Positioning

Ideally infants should be positioned to provide a good video image of limbs, face, and trunk. However, infants may be positioned by nursing or attending physician staff for other clinical purposes. There may be a number of constraints in maintaining a good video image: Limbs with intravascular line placements may be restrained; agitated infants may be swaddled; some infants may be intubated with limited range of head and neck movement; there may be wound dressings; infants must remain covered because of temperature instability. These and other problems must be addressed to obtain the best video image for each study.

Camera Mount

The camera mount must be stable and must not "jitter" or bounce with the movement of personnel around the EEG instrument. In addition, it is best that the camera be mounted so that it is directly above the neonate to provide a full view of all limbs and the head without the distortion that comes from a camera placed at the foot or to the side of the infant. However, most commercially available camera and camera mount systems are vertical to the EEG instrument and provide lateral or foot-of-the-bed views of the infant.

Lighting

Lighting in neonatal special care areas can be suboptimal for video recording. Ambient light is dictated by clinical needs and day/night cycles imposed for optimal infant adaptation. Most commercially available cameras have low-light capability that allow for adequate video images. When additional light is used to enhance picture quality, additional problems may arise. Added light may provide added heat and cause the infant to perspire enhancing sweat artifact. Added light may also provide stark shadows and obscure the image of limbs.

Potential for Missed Events

A potential is always present for missing the video recording of important paroxysmal clinical events. The optimal video recordings are those time-linked with EEG, but much can be determined from the video image alone. To maximize video recording yield, the ENDT must first arrange the video camera and begin video recording. This can start immediately after the EEG instrument is brought to the bedside or the infant is brought to the laboratory. Video recording continues through the gathering of historical data and preparation of the infant for EEG. It is terminated only after all electrodes are removed and the infant is cleaned and the instrument is removed. In this way clinical events that may occur before or after the EEG recording may be captured.

RECORDING PROTOCOLS

The most successful and clinically relevant neonatal EEG recordings are those in which objectives and strategies are identified prior to the beginning of each study. Advance planning is essential. This can be based upon a basic algorithm adaptable to individual recording circumstances (**Figure 2.2**). The basic tasks are to obtain historical data, determine reason for referral, initiate technical recordings, examine the EEG in real time, observe the infant for clinical behaviors, record the infant in sleep and wakefulness, and attempt to provoke abnormal paroxysmal clinical events.

Close observation of the infant at all times is particularly important when recording a neonatal EEG. The record should be annotated when behavioral, physiologic, or autonomic changes occur or when other events happen that may affect the record. It is important that the technologist and clinical neurophysiologist know what behaviors are thought by the referring physician to be clinical seizures. In addition, if the type of paroxysmal behavior for which the infant was referred occurs during the recording, the event should be noted and described. Other abnormal behaviors should also be noted on the record at their time of occurrence.

Some behaviors thought to be seizures can be elicited by tactile stimulation and suppressed by restraint or repositioning of the infant's limbs or trunk. Therefore, bedside maneuvers to elicit or suppress such clinical behaviors are essential to an adequate recording of the neonatal EEG. During the recording, infants suspected of having seizures should be subjected to proprioceptive or tactile stimuli or repositioning of the head, trunk, or extremities. When tonic posturing or motor automatisms occur, the ENDT should determine if they can be stopped by repositioning the head, trunk, or limbs. If stimulation elicits abnormal behavior, it is important to determine the relationship between the intensity of the stimulus and the intensity and irradiation of the response. It should also be determined whether the intensity of the behavior or the degree of irradiation can be increased by stimulating at multiple sites or by repetitive stimulation of the same site. Finally, attempts should be made to suppress abnormal movements with light restraint (Kellaway and Hrachovy, 1983; Mizrahi and Kellaway, 1987).

An important concern is the duration of the neonatal EEG recording. There are two considerations: the time it may take for the infant to experience the full cycles of sleep and wakefulness and a sufficient period of time for the infant to experience clinical events or electrical seizures. The

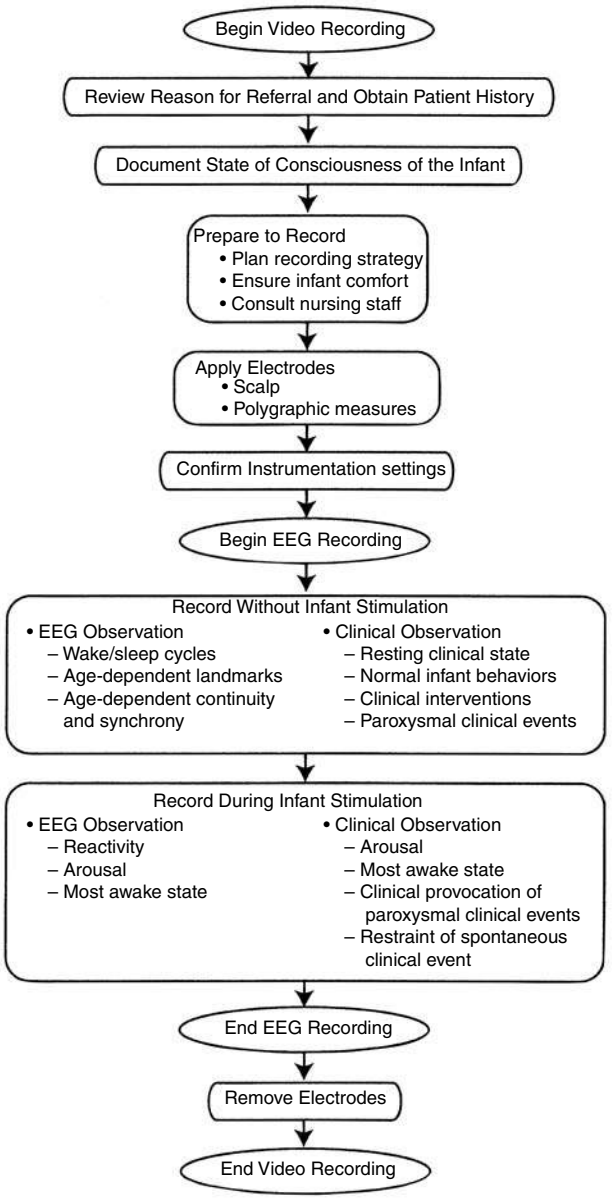

Figure 2.2 Flow diagram of the sequence of recording neonatal EEG with video. If video is not used, only those steps related specifically to video are eliminated, and the remainder of the steps is followed for EEG recording.

typical minimum duration of recording for a neonatal EEG is 1 hour in the TCH neurophysiology laboratory. A recording may be longer in an infant who may be particularly irritable and may take more time to fall asleep. Conversely, circumstances for a critically ill infant may require that the recording time be shortened. However, even a critically ill infant who is comatose and who may have an EEG that is depressed, undifferentiated, and nonreactive to stimulation may require a recording of at least a full hour since electrographic seizures may occur. Thus, the determination of recording duration is an interactive process based upon clinical circumstances and the unfolding EEG.

PROLONGED EEG-VIDEO MONITORING

There is an increasing interest and clinical need for the prolonged monitoring of neonates with EEG and video for seizure surveillance, the real-time consideration of the degree of diffuse brain injury, and during specialized therapies such as hypothermia. Guidelines for monitoring and terminology use for neonates have been developed by the ACNS (Shellhaas et al., 2011; Tsuchida et al., 2013). Technical considerations described earlier apply, although there are additional considerations regardless of whether video is used, or EEG alone is monitored (Boylan et al., 2013; Chang and Tsuchida, 2014; Lloyd et al., 2015; McCoy and Hahn, 2013; Shellhaas, 2015). As with any EEG study, diagnostic and therapeutic goals need to be defined. An initial target of duration of monitoring should be defined and then periodically reassessed. Electrodes should initially be placed according to standard guidelines with the recognition that this may be modified according to other diagnostic and therapeutic needs (e.g., repeated head ultrasound studies may mean midline central electrodes are displaced). The sites of the placement of individual electrodes must be inspected on a regular basis to monitor for the presence of skin breakdown.

Plans for recording surveillance and reporting of results should be in place prior to onset of monitoring. Decisions should be made concerning which staff will provide real-time interpretation, how the neurophysiologist will be continuously engaged, how frequently formal reports will be generated, and how the neurophysiology team and neonatalogy/neurology teams interact. Parameters need to be established to indicate what therapeutic action may be taken if specific findings are observed. Storage of data has become an important issue and should be consistent with home institution policy. Recent guidelines for monitoring of adults and children provide more detailed parameters for data storage (Herman et al., 2015a, 2015b).

CHAPTER 3

Artifacts

The differentiation of true brain electrical activity from extraneous artifacts is critical to the interpretation of neonatal electroencephalogram (EEG). Traditionally, the sources of artifacts are considered in four broad categories: environment, instrumentation–patient interface, instrumentation, and physiologic potentials of noncerebral origin (Brittenham, 1990; Dworetzky et al., 2011; Kellaway and Crawley, 1964; Saunders, 1979; Scher, 1985).

The identification of artifacts in a given EEG recording is a two-step process. The first occurs during the actual recording and is dependent upon the electroneurodiagnostic technologist's (ENDT) recognition of artifacts and their potential sources. With this recognition, it is the ENDT's task to isolate the source and resolve the problem. If this proves impossible, the ENDT will make appropriate notations on the record and on the accompanying log to characterize the activity and suggest the source. The second step of artifact identification occurs during interpretation of the EEG. Since artifacts may mimic true brain-generated waveforms (**Tables 3.1–3.5**), the challenge lies with the clinical neurophysiologist to make the accurate and appropriate distinctions.

Table 3.1 Sources of Artifacts That Can Mimic EEG Focal Asymmetries

- Instrument–patient interface
  - Asymmetric electrode placement
- Instrumentation
  - Settings
- Physiologic
  - Asymmetric scalp edema
  - Skull defects

Table 3.2 Sources of Artifacts That Can Mimic Focal Slow Activity That Is Either Random or Rhythmic

- Instrument–patient interface
  - Inadequate electrode contact
  - Head positioning
  - Spontaneous or passive body, limb, or head movements
  - Pulse
  - Respiration
- Physiologic
  - Endogenous electrical potentials
    - Tongue movements
    - Eye movements

Table 3.3 Sources of Artifacts That Can Mimic Sharp Waves or Spikes That Are Either Random or Rhythmic

- Instrument–patient interface
  - Inadequate electrode contact ("pop")
  - Spontaneous or passive movements
    - Sucking, burping, hiccupping
- Physiologic
  - Electrocardiogram (ECG or EKG)
  - Electrooculogram (EOG)
  - Facial electromyogram (EMG)
- Environment
  - Infusion pumps
  - Ventilator
  - Extracorporeal membrane oxygenation (ECMO)
  - Cellular telephones, radio transmitters

Table 3.4 Sources of Artifacts That Can Mimic Generalized Activity That Is Either Paroxysmal or Sustained

- Instrumentation–patient interface
  - Spontaneous and passive movements
    - Rocking, patting
- Instrumentation
  - Swaying of electrode leads
- Physiologic
  - Sweating
- Environment
  - 60-Hz interference from adjacent instruments

Table 3.5 Sources of Artifact That Can Mimic Generalized Voltage Depression

- Instrumentation
  - Instrumentation settings
- Physiologic
  - Diffuse scalp edema

ENVIRONMENT

Although the EEG laboratory is a relatively controlled electrical environment, the neonatal intensive care unit (NICU) is relatively uncontrolled. This is due to the wide number of instruments used to monitor or care for infants including phototherapy lights, ultrasound instrumentation, infusion instrumentation accessing the intravascular system at various sites, and extracorporeal membrane oxygenation (ECMO) pumps (**Figures 3.1–3.3**). Electrical artifact due to external currents from these instruments may appear in all EEG channels to the same degree or may appear focally. When all of the electrode impedances are equal, the more likely the environmental current will be expressed in all channels; unequal impedances will cause the current to be expressed to a greater degree or exclusively in those channels with the highest impedance.

Additional environmental artifacts may be created or enhanced by factors such as capacitatively induced potentials from electrode wires that sway or electrostatic potentials resulting from movement of personnel around the recording area. Malfunctions and/or improper operation of equipment such as monitors connected to the patient can also result in artifactual signal induced into the EEG machine.

Oscillatory ventilators may induce relatively high-frequency electrical artifacts compared to more traditional ventilator systems. Thus, rate alone cannot be used to exclude potentials suspected of being generated by a ventilator.

Cellular telephones and older radio transmitters can sometimes produce artifactual signals in the EEG tracing, especially if these devices are operated within a few feet of the patient.

RECORDING INSTRUMENTATION–PATIENT INTERFACE

The interface between the recording instrument and the patient is at the electrode site. Inadequate or unstable contact between the electrode surface and the skin may result in a sudden change in the junction potential and/or impedance that can produce extraneous potentials in affected channels. These may appear as single or repetitive rapid, spike-like waves with an abrupt upward initial phase (the so-called "electrode pop") (**Figures 3.4–3.7**). In addition, asymmetry of the site of placement of homologous electrodes may result in significant voltage asymmetries in the EEG.

The electrode interface may also be altered by the degree to which the infant may perspire. Diffuse sweating may result in long duration potentials that initially appear as generalized or regional slow activity (**Figures 3.8** and **3.9**). Very slow potentials may occur due to changes caused by alterations in surface electrolyte compositions—these potentials are similar to the galvanic skin response.

Movement of the head against the bed due to respirations or other body movements may produce sharp and/or slow potentials arising from that particular electrode (**Figures 3.10** and **3.11**). Pulse may also cause a recorded artifact by production of movement in a region adjacent to an electrode site. The head may also be moved by mechanical devices such as a ventilator or ECMO pump (**Figures 3.12** and **3.13**). This is due to a mechanical, or ballistic, movement induced by the instrument—a cause of artifact from these devices different from electrical interference described earlier.

Other body movements may also alter the patient–electrode interface and result in artifacts. These include limb movements that may be random, purposeful, or associated with clinical seizures and other limb or body movements (**Figures 3.14–3.18**). In addition to the movements that may be caused by the infant, the infant may be moved or manipulated during comforting, feeding, medical procedures, and in the course of treatments. Movements created to comfort the infant may be particularly troublesome, such as rocking, patting, and burping the infant (**Figures 3.19–3.23**).

RECORDING INSTRUMENTATION

The recording instrument itself can be a source of artifacts. These may be the result of malfunction at any recording level. When analog-type EEG instruments were used they were subject to pen misalignment and excessive damping. Digital recordings may have problems relating to malfunction of the operating systems. There is also the potential for human error in the use of any recording device. Settings for EEG channels may not be uniform, electrodes may not be correctly plugged in, and montages may not be accurately selected.

NONCEREBRAL PHYSIOLOGIC POTENTIALS

Alterations in Electrical Properties of Scalp or Skull

There may be differences in impedance and volume conduction properties over various regions of the scalp due to scalp edema. The edema may be the result of transit through the birth canal, more significant birth or other trauma, placement of intravenous lines with or without extravasation of fluid, the placement of a ventriculoperitoneal shunt, or the presence of a surgical wound. If edema is diffuse, this may lead to a pattern of background activity that is low in amplitude in all regions. If the edema is regional or asymmetric, this may lead to a pattern of focal depression, suggesting a focal lesion if the edema is not noted. There may also be instances in which conductive properties are altered because of the absence of underlying skull, typically (although rarely) in the case of cranial surgery. A skull defect creates a preferential pathway for electrical current, resulting in increased amplitude of EEG activity over the affected region.

Vital Signs Monitoring

Heart rate and respiration are important sources of artifact on EEG. The electrocardiogram (ECG) in an infant may appear as a contaminant in one, some, or all of the EEG channels (**Figures 3.24–3.27A,B**). It may be constant or intermittent. Respirations may also appear as artifact, whether spontaneous or driven by a ventilator. These artifacts may be unilateral or bilateral, depending upon body and head position.

Movements

Some movements by the infant can produce a number of endogenous electrical potentials that can be reflected in EEG channels. These movements include oral-buccal-lingual movements such as sucking and tongue thrusting (i.e., glossopharyngeal potential); paroxysmal pharyngeal movements such as hiccupping and spontaneous burping (i.e., pharyngeal muscles and diaphragmatic electromyography [EMG]); and jaw tremor (**Figures 3.28–3.34**); ocular movements such as eye deviations, blinking and repetitive eye opening, and closure (i.e., electrooculogram) (**Figures 3.35–3.38**); and chewing, lip-smacking, or other facial movements (i.e., temporalis frontalis or other facial muscle EMG) (**Figures 3.39–3.45**) or body movements (**Figure 3.46**).

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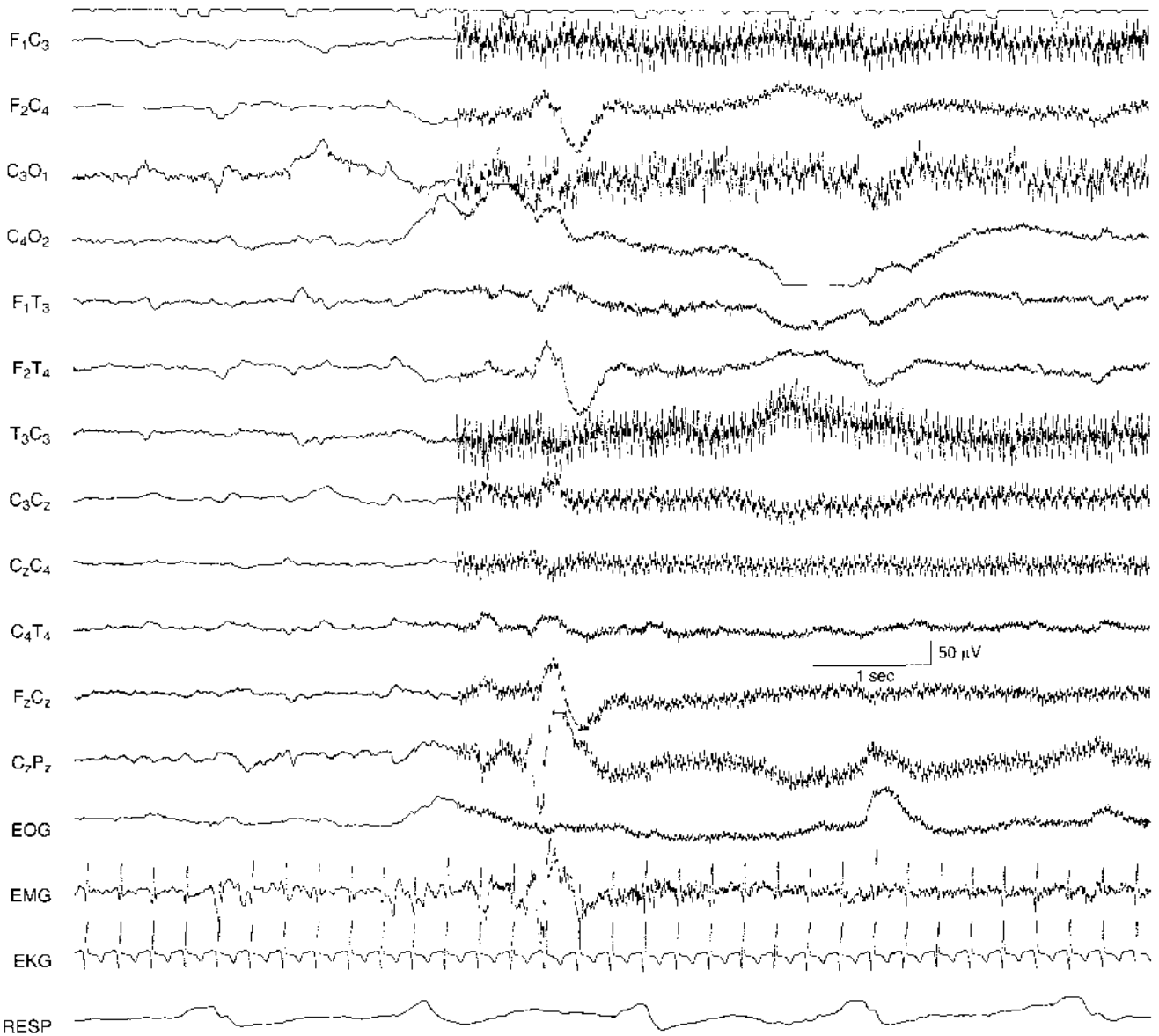

Figure 3.1 Electrical interference due to mechanical device. Electrical interference is present in all leads when an infusion pump for intravenous fluids is activated at the bedside. The interference is modified in this instance by the use of a 60-Hz filter. The EEG background activity is depressed and undifferentiated in this full-term infant.

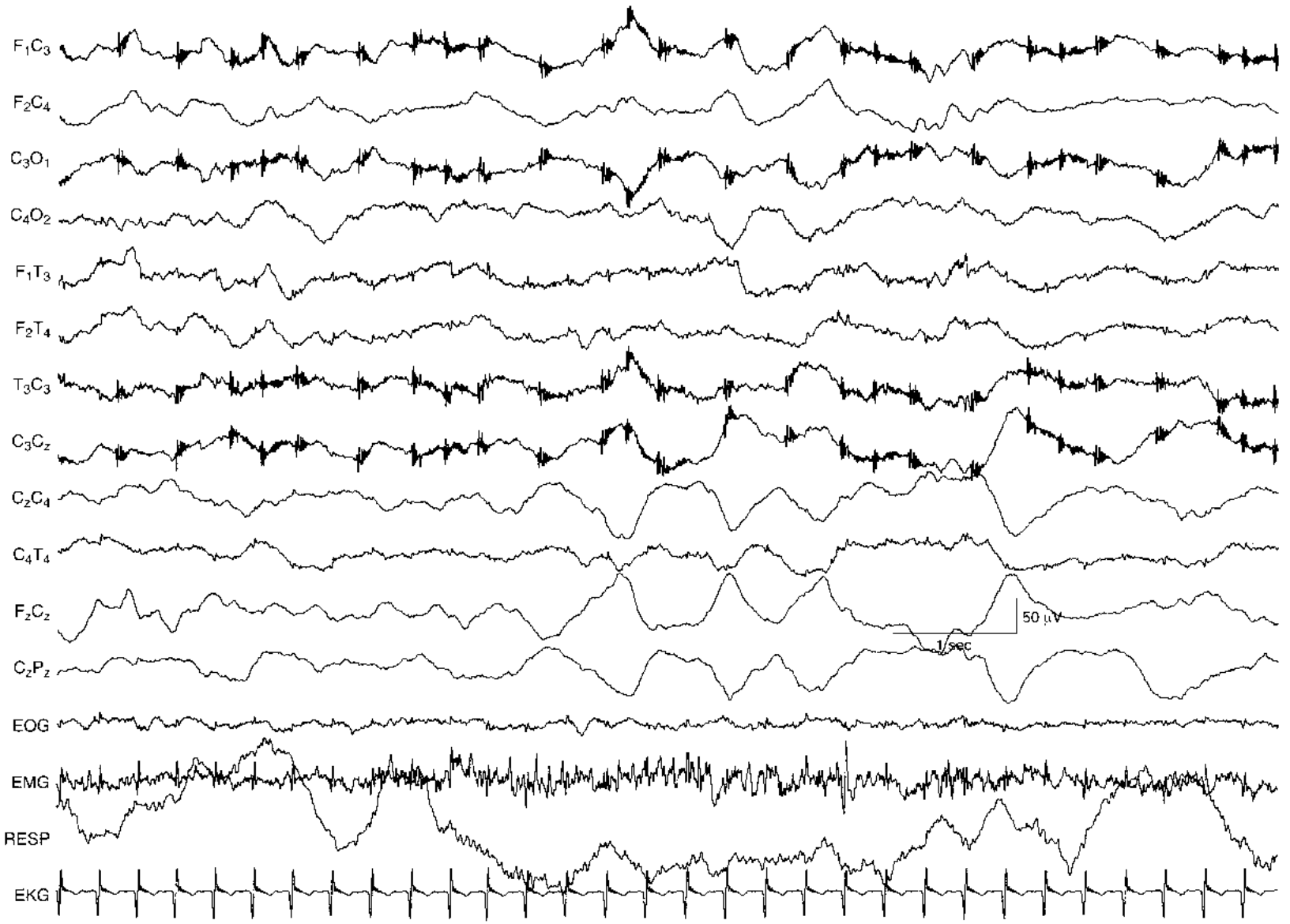

Figure 3.2 Electrical interference due to ICU instrumentation. Electrical artifact is present in channels involving the C3 electrode that has relatively high impedance compared to others. This 40-week CA infant was cared for in an intensive care unit (ICU) with monitors, ventilator, and infusion pump.

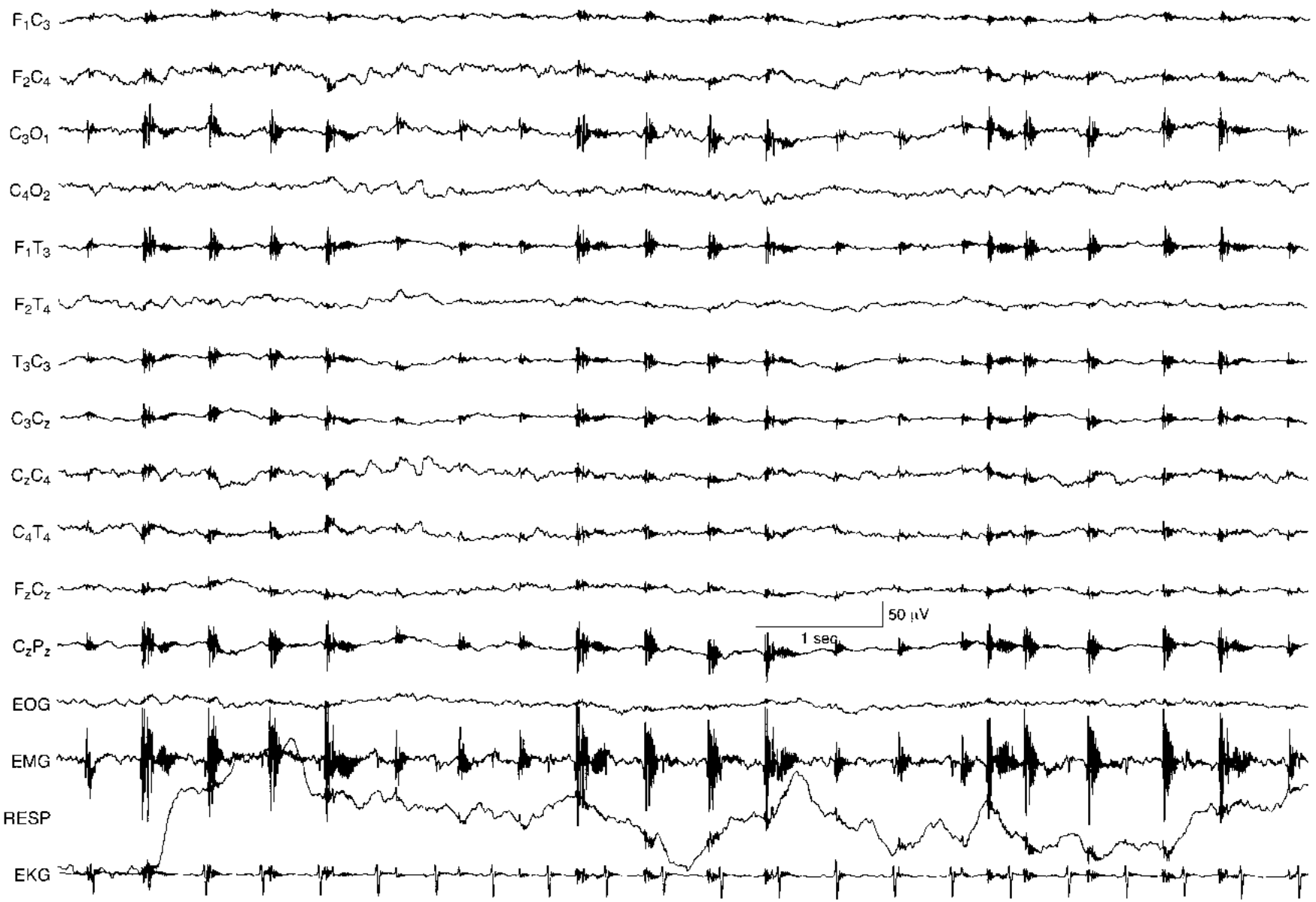

Figure 3.3 Periodic electrical interference due to mechanical device. Periodic bursts of electrical interference are due to an extracorporeal membrane oxygenation (ECMO) pump used to support this term infant, whose background EEG is depressed and undifferentiated. The bursts correlate with rotations of the pump.

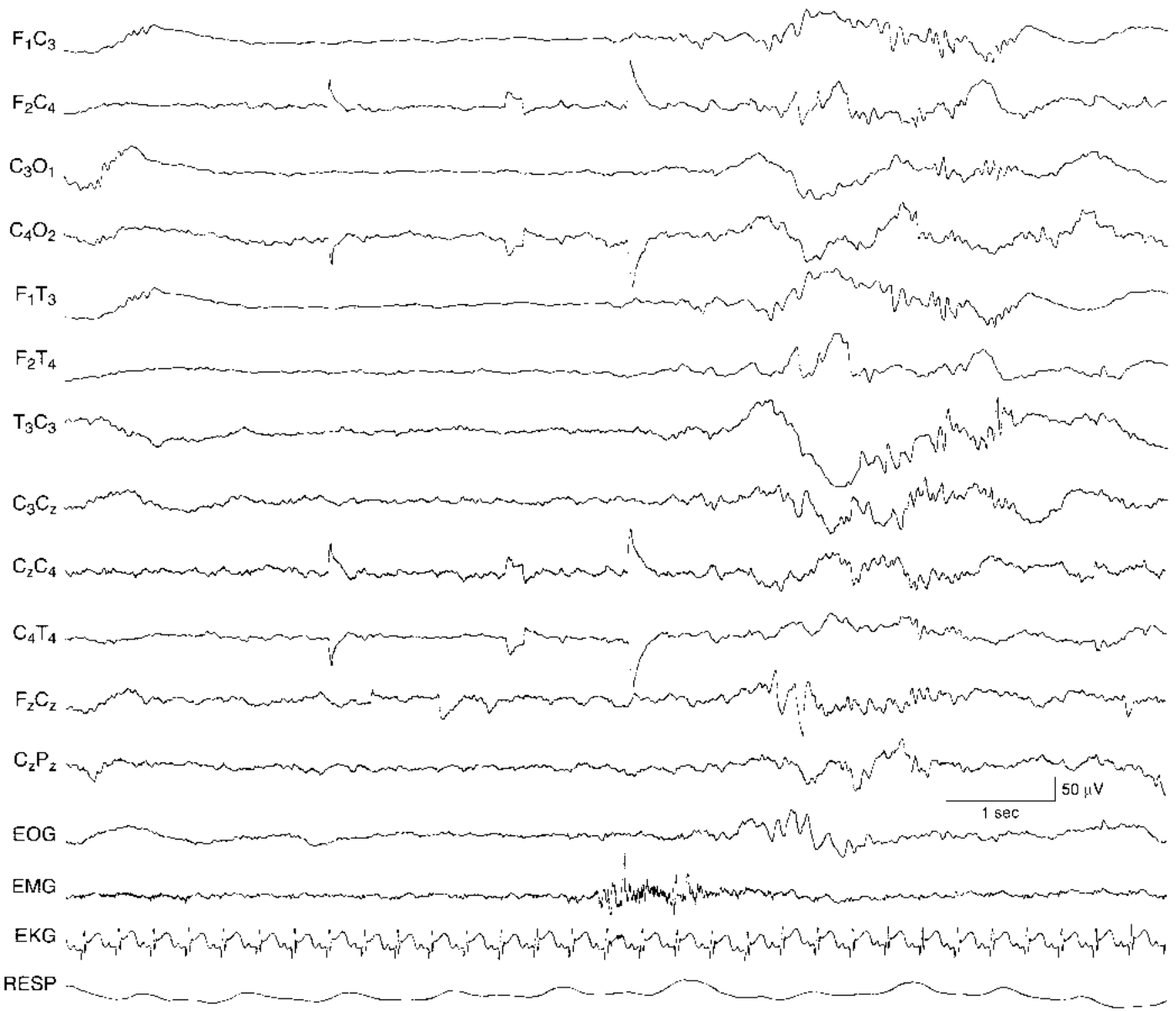

Figure 3.4 Electrode "pop." An unstable electrode at C4 has resulted in a characteristic waveform with a steep initial component, sharp morphology, and more gradual return to baseline. This occurred in a 36-week CA infant whose background EEG is characterized by a suppression-burst pattern.

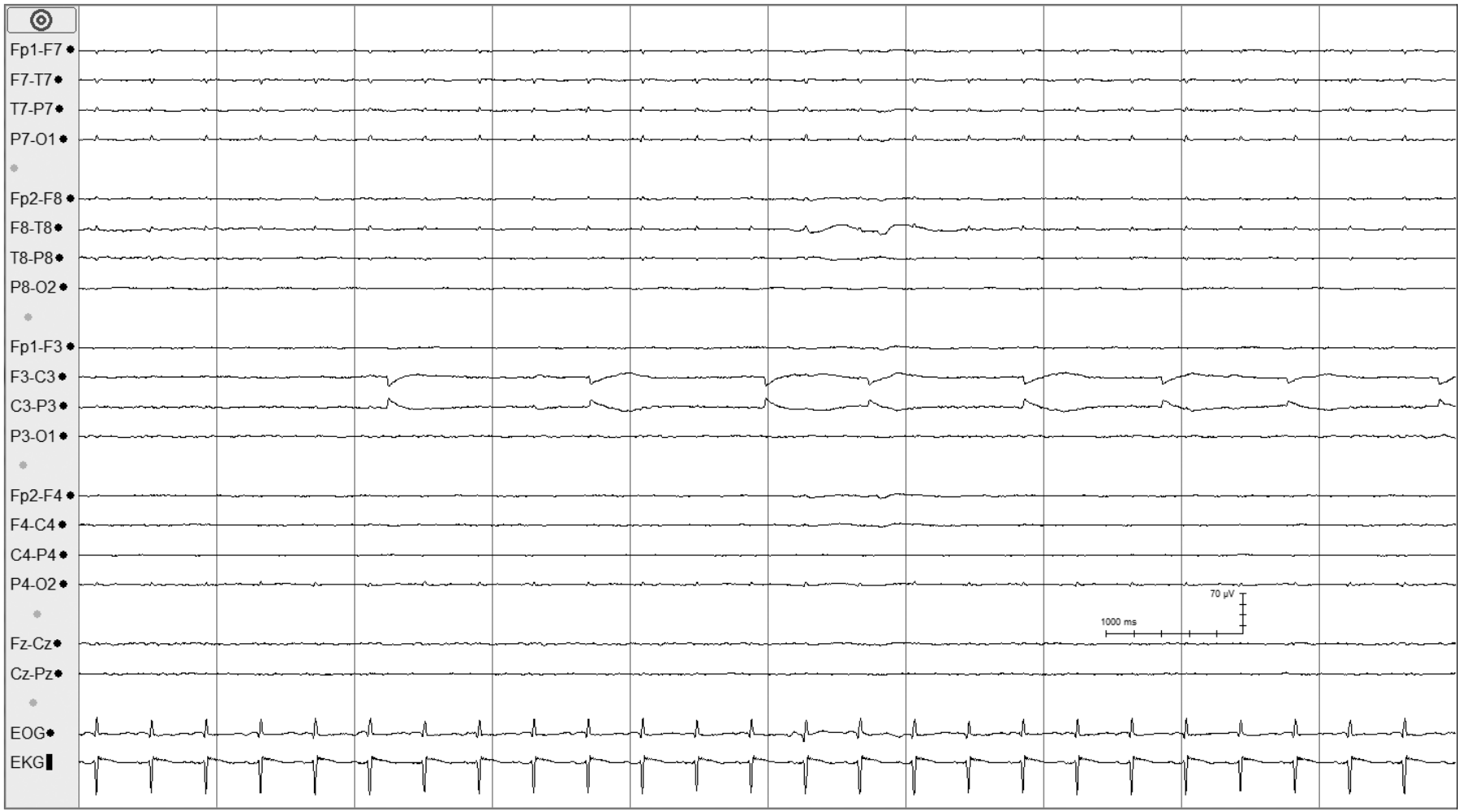

Figure 3.5 Recurrent electrode "pop" at C3. Recurrent, slowly repetitive, sharp waves are present in the left central region due to electrode instability. Each waveform begins with a steep deflection typical of electrode "pop." The background activity is depressed and undifferentiated in this 39-week CA infant with hypoxic ischemic encephalopathy.

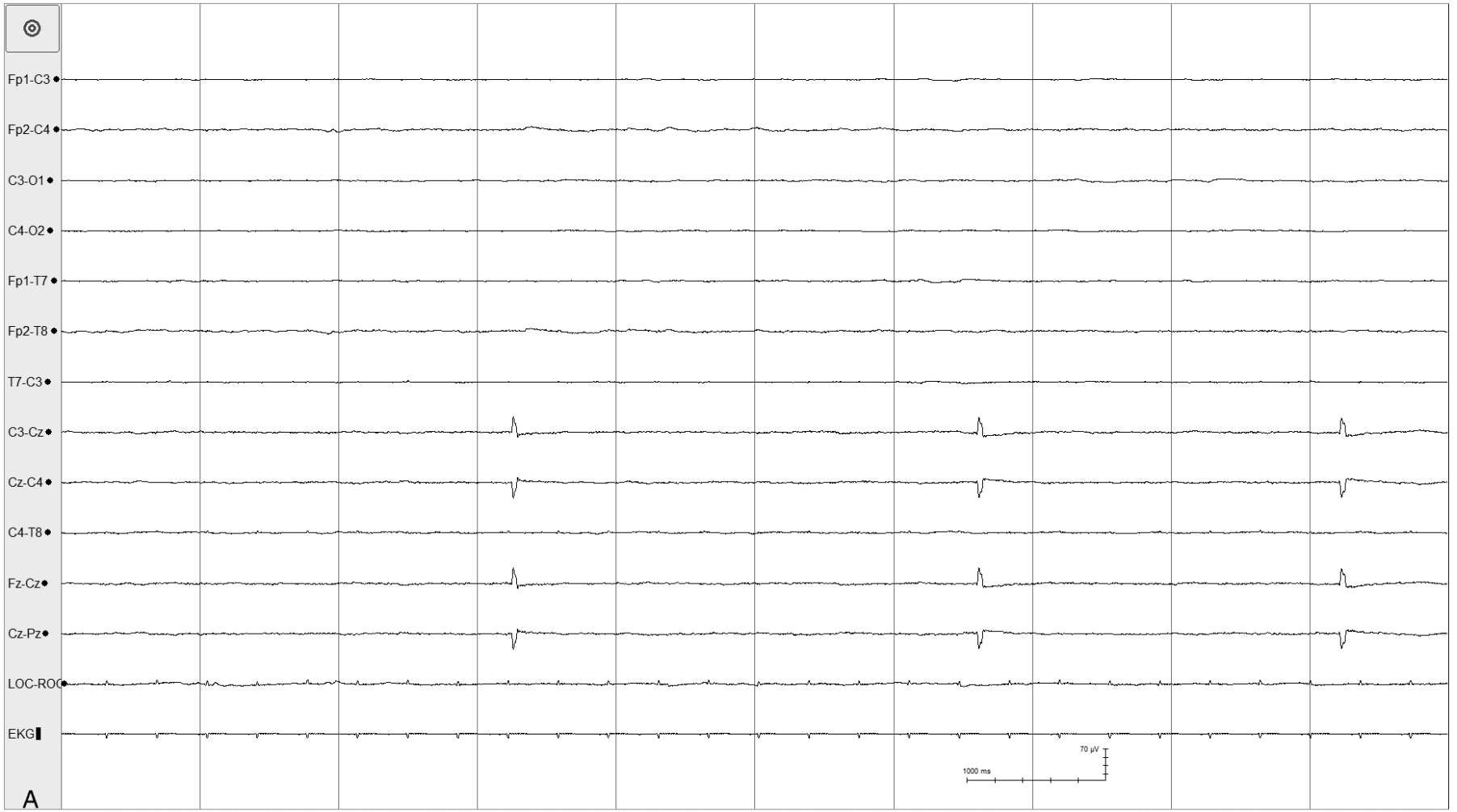

Figure 3.6 (A)–(E) Electrode instability at Cz. Recurrent positive sharp waves are present in the midline central region due to instability of the Cz electrode which resulted in characteristic rapidly deflected waves with varying morphology and recurrence rate in a 26-week CA infant during a period of an abnormally prolonged interburst interval. (*continued*)

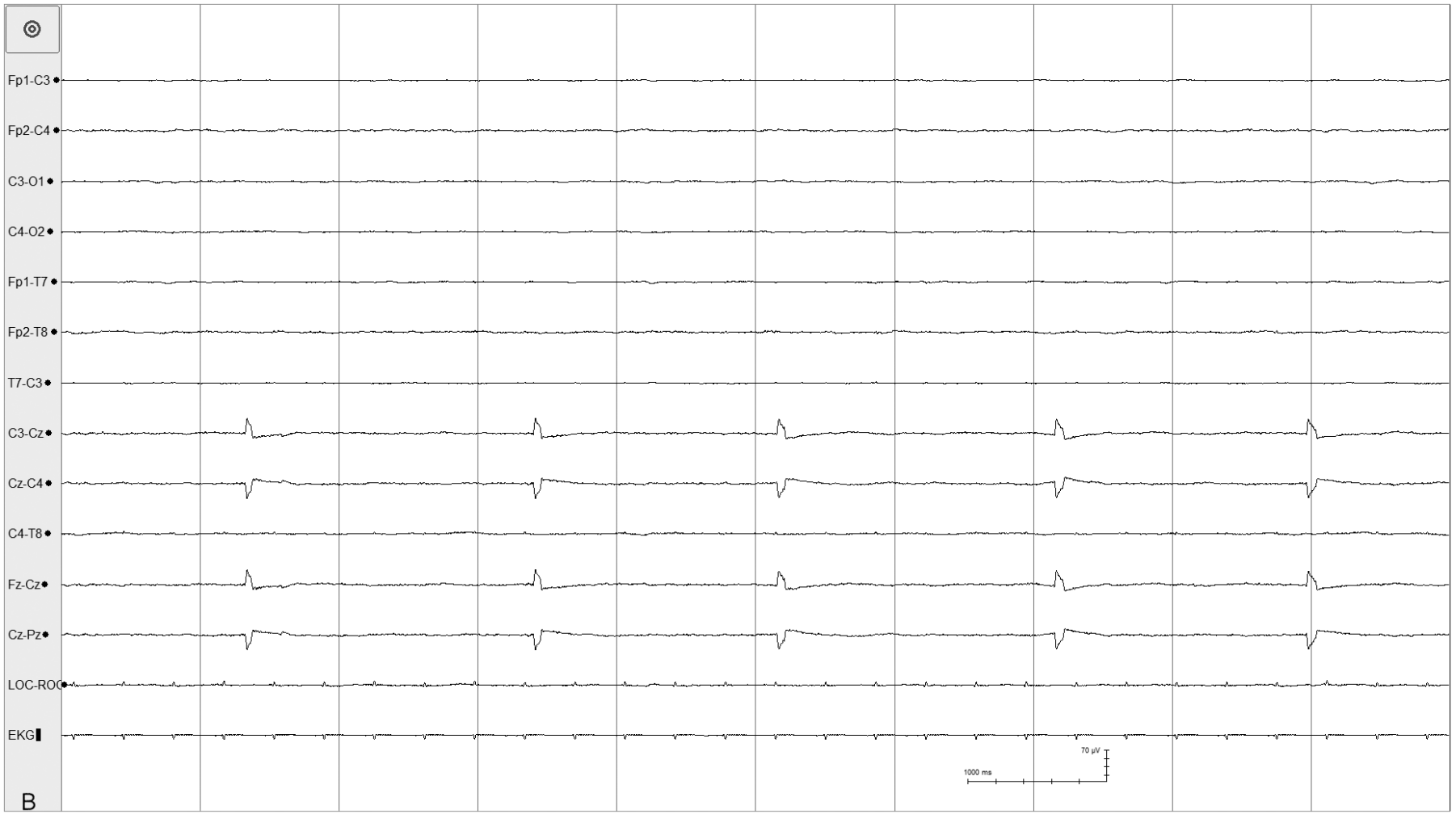

Figure 3.6 (*continued*)

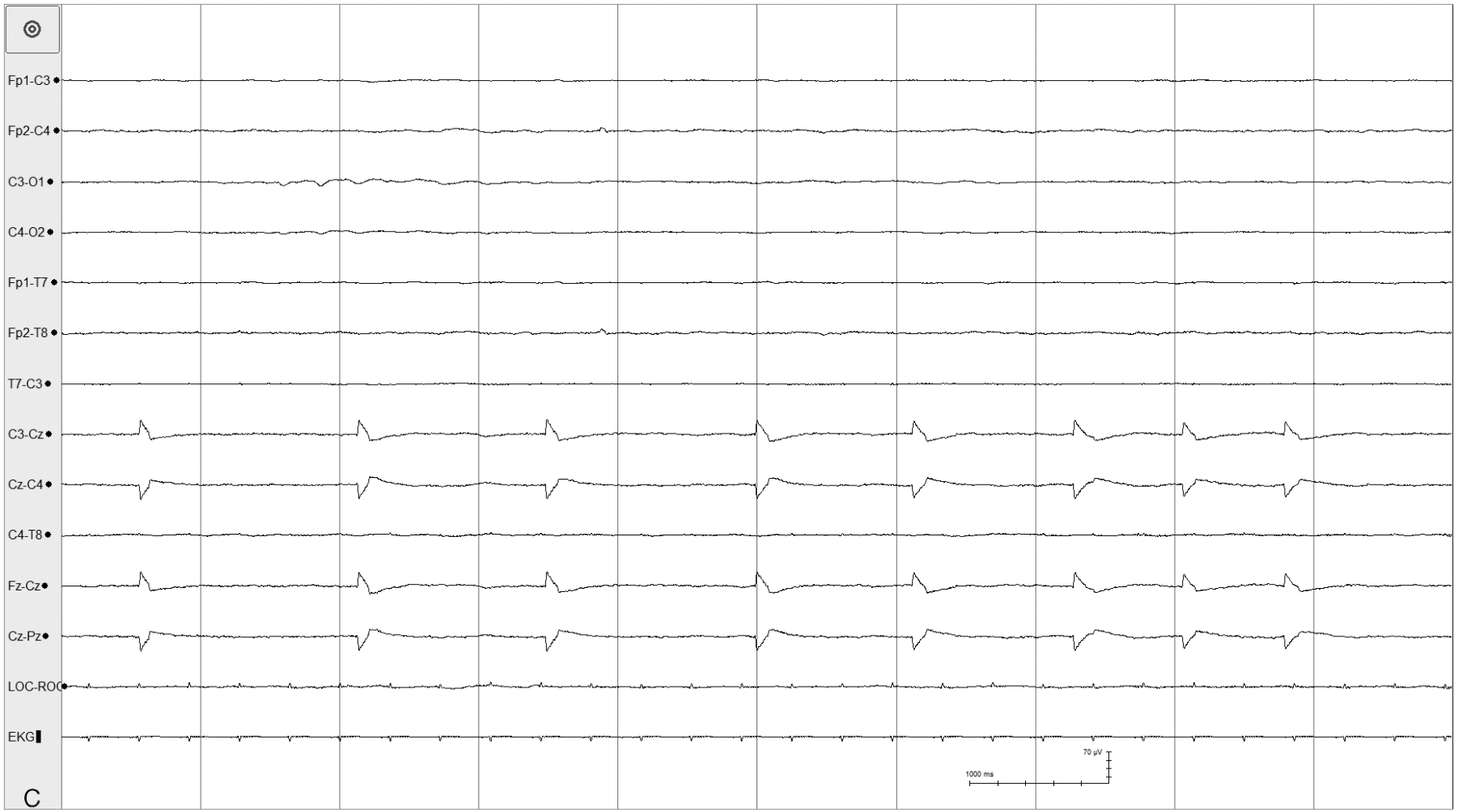

Figure 3.6 (*continued*)

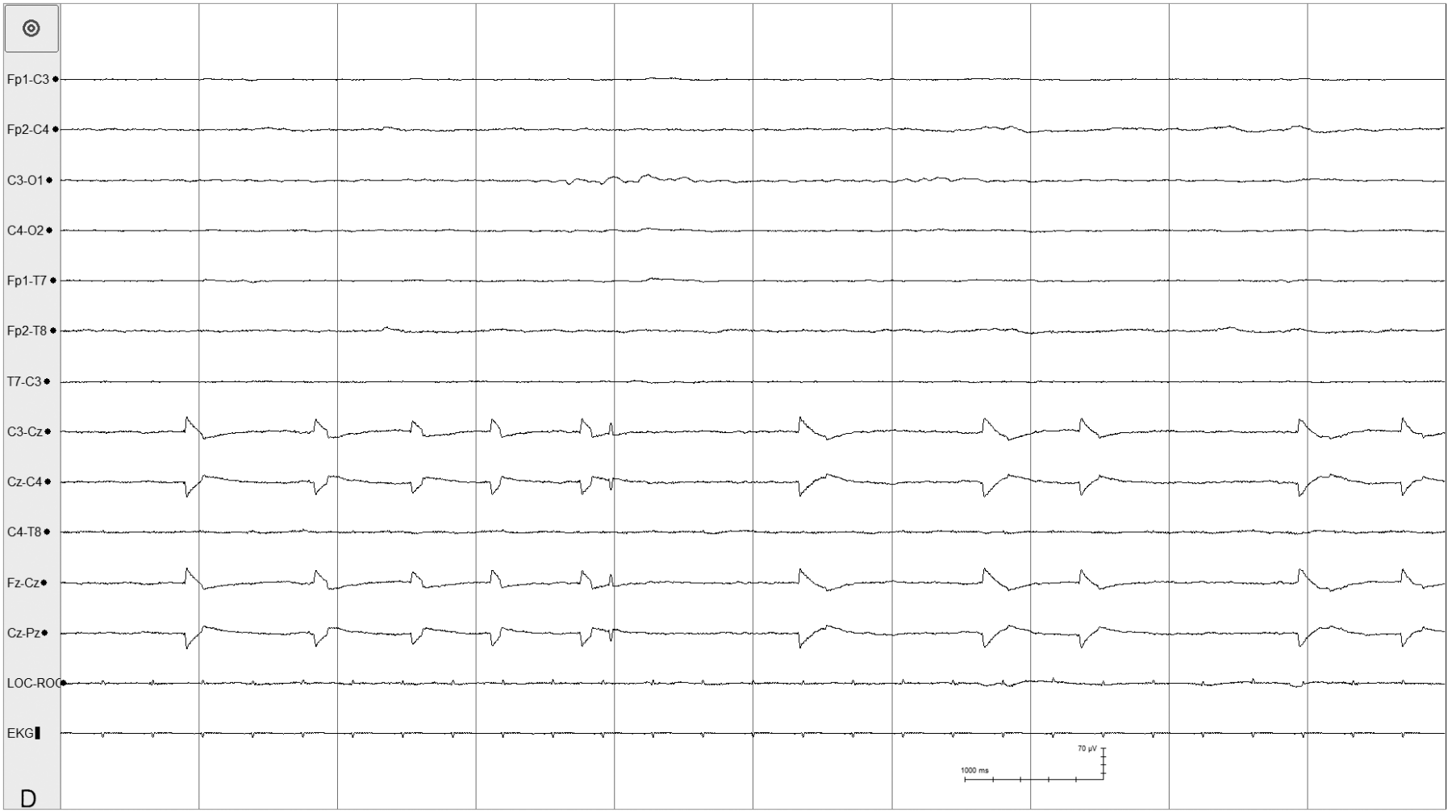

Figure 3.6 (*continued*)

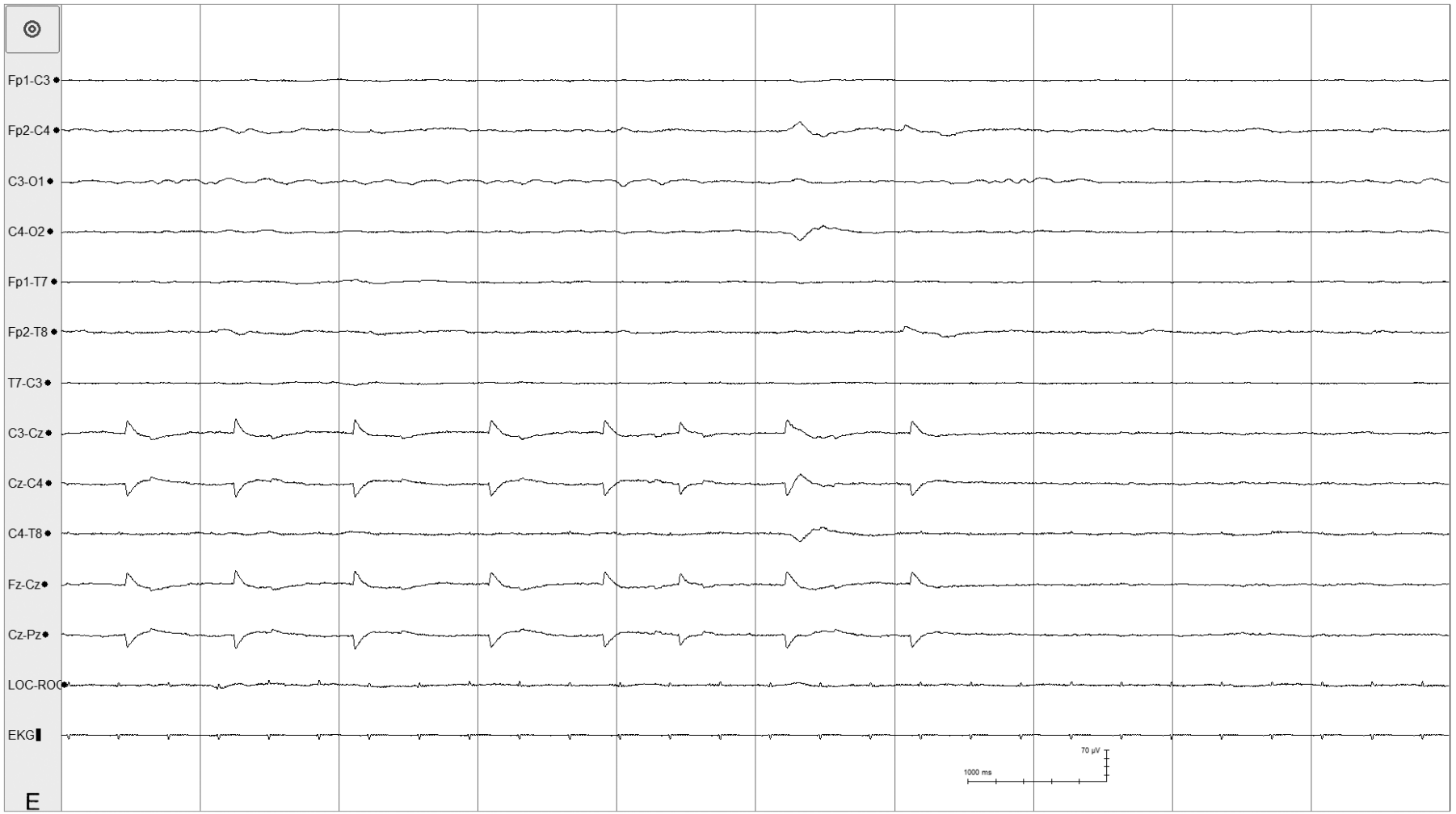

Figure 3.6 (*continued*)

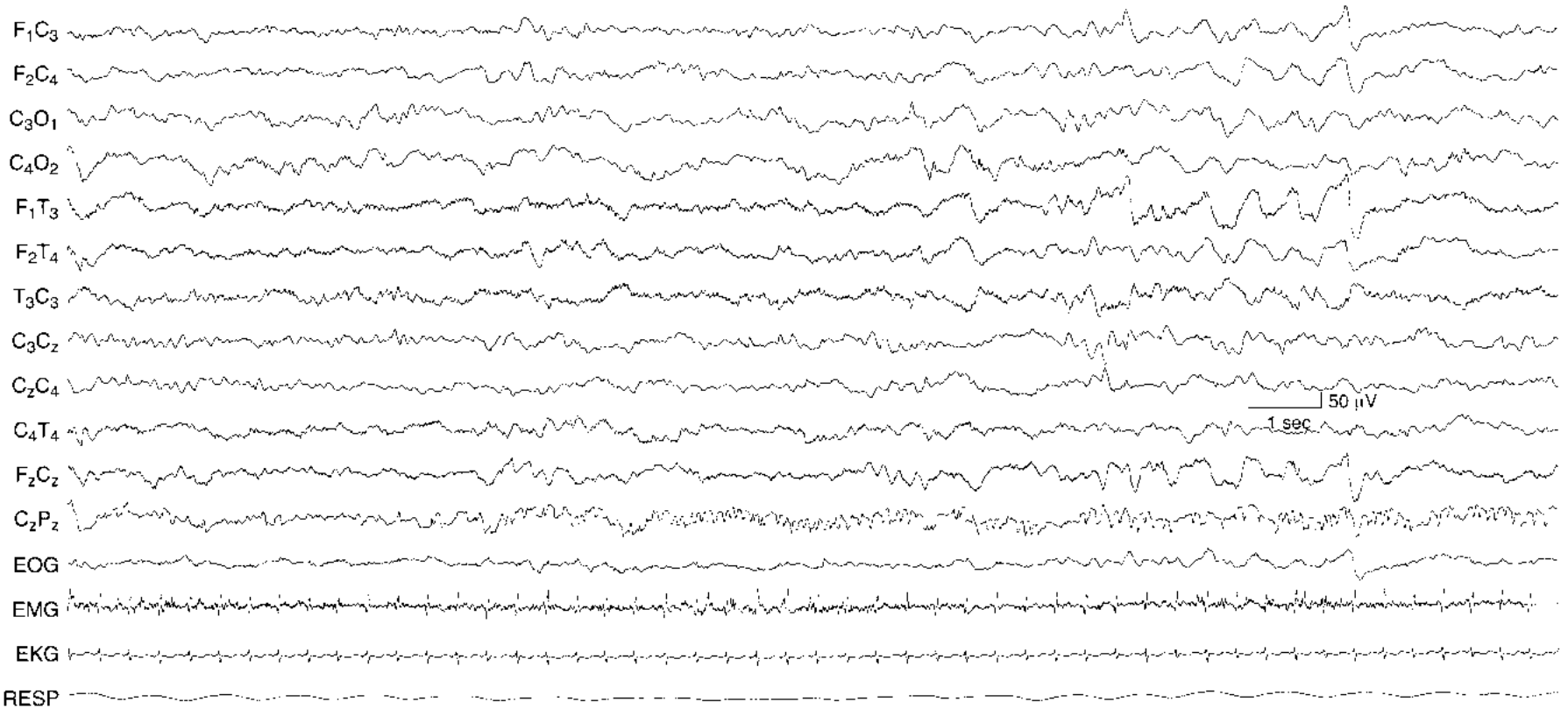

Figure 3.7 Irregular, sustained waveforms due to unstable electrode. The Pz electrode in this recording has become unstable resulting in irregular, sustained, low voltage, relatively fast activity. Some of the waveforms have a nonphysiologic, angular, and square morphology. This occurred in a 42-week CA infant whose background EEG activity is normal.

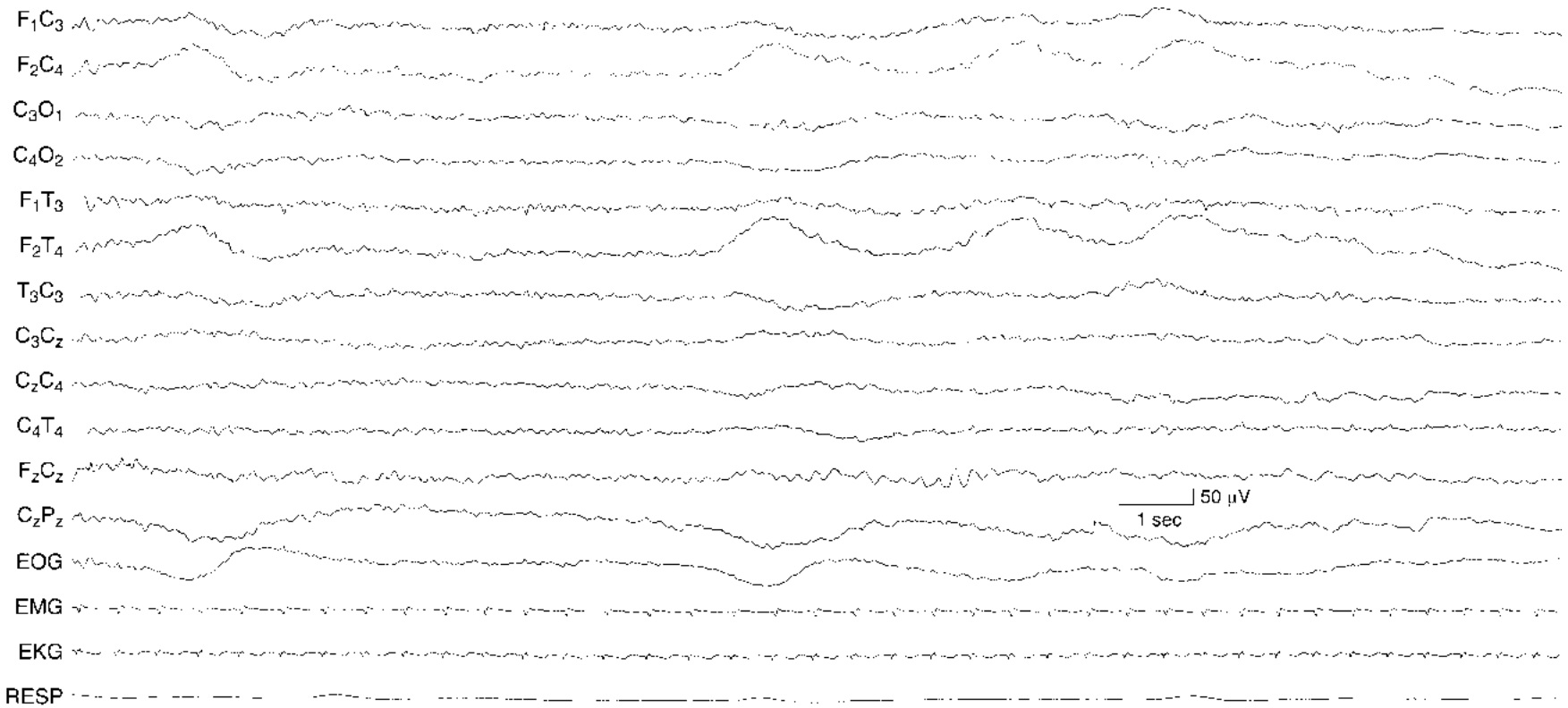

Figure 3.8 Intermittent, high amplitude, long duration potentials due to sweat. High voltage, long duration waveforms are present, predominantly in the right frontal central region due to excessive sweating of this 40-week CA infant with normal background EEG activity.

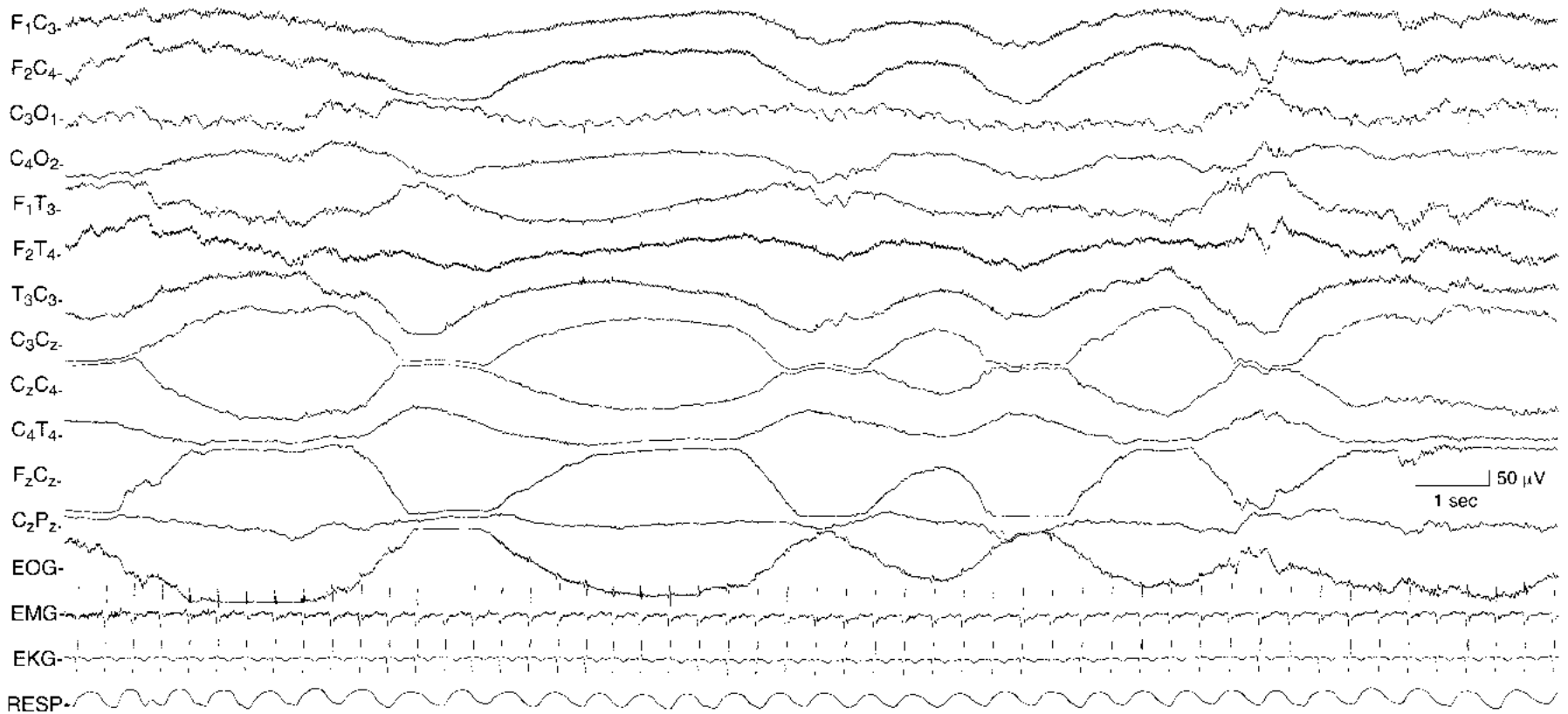

Figure 3.9 Sustained, high amplitude, long duration potentials due to sweat. The high voltage, long-duration waveforms are predominantly in frontal and central regions and are sustained. This activity is due to excessive sweating of the infant. There is also EKG reflected in leads chiefly from the left occipital and EMG in anterior leads. This infant is 40-week CA with a background EEG that is depressed and undifferentiated.

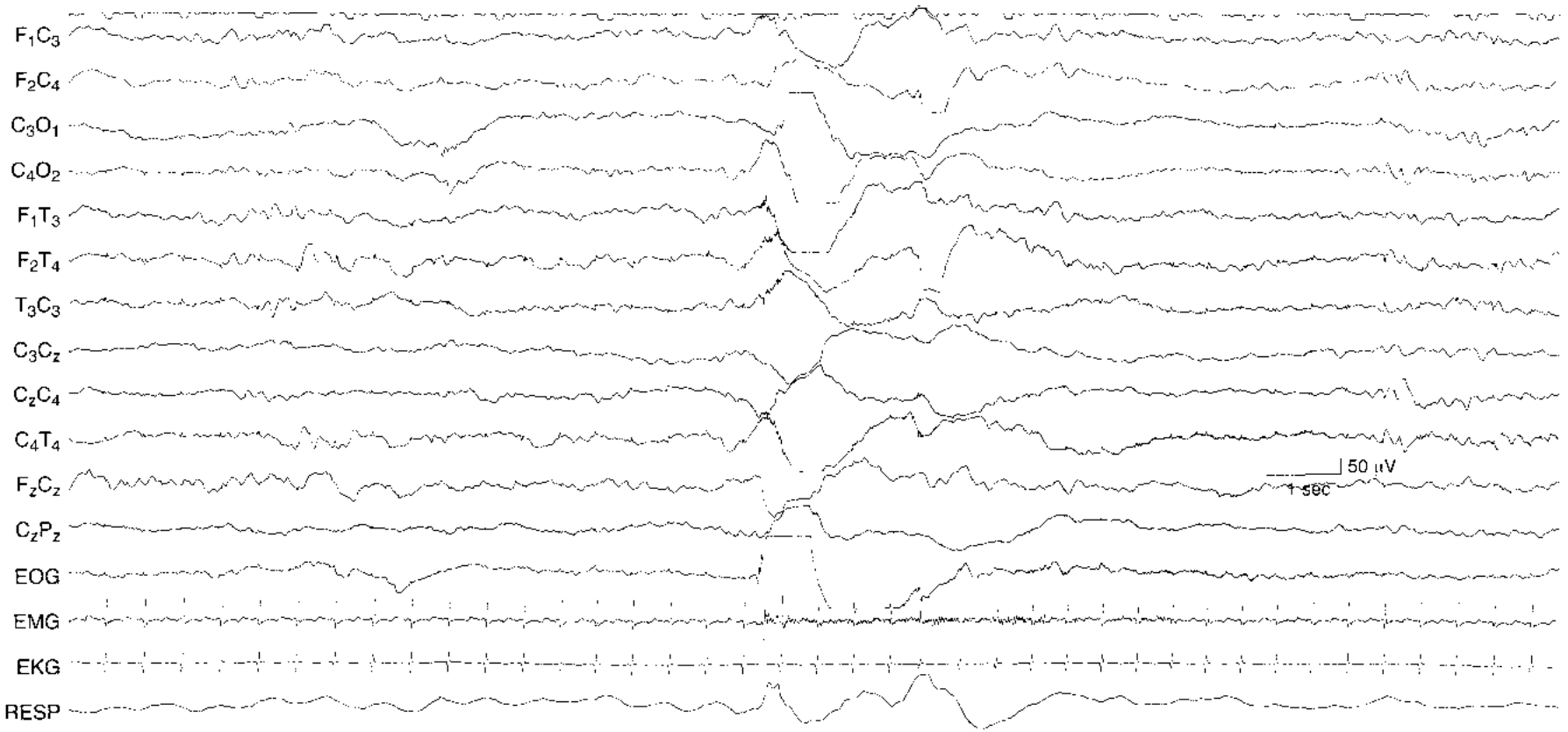

Figure 3.10 High amplitude, long duration, asynchronous potential due to head movement. Spontaneous head movement has resulted in high amplitude, slow waves appearing in leads from both hemispheres, with some asynchronous components on the two sides in this 41-week CA infant with normal background EEG activity.

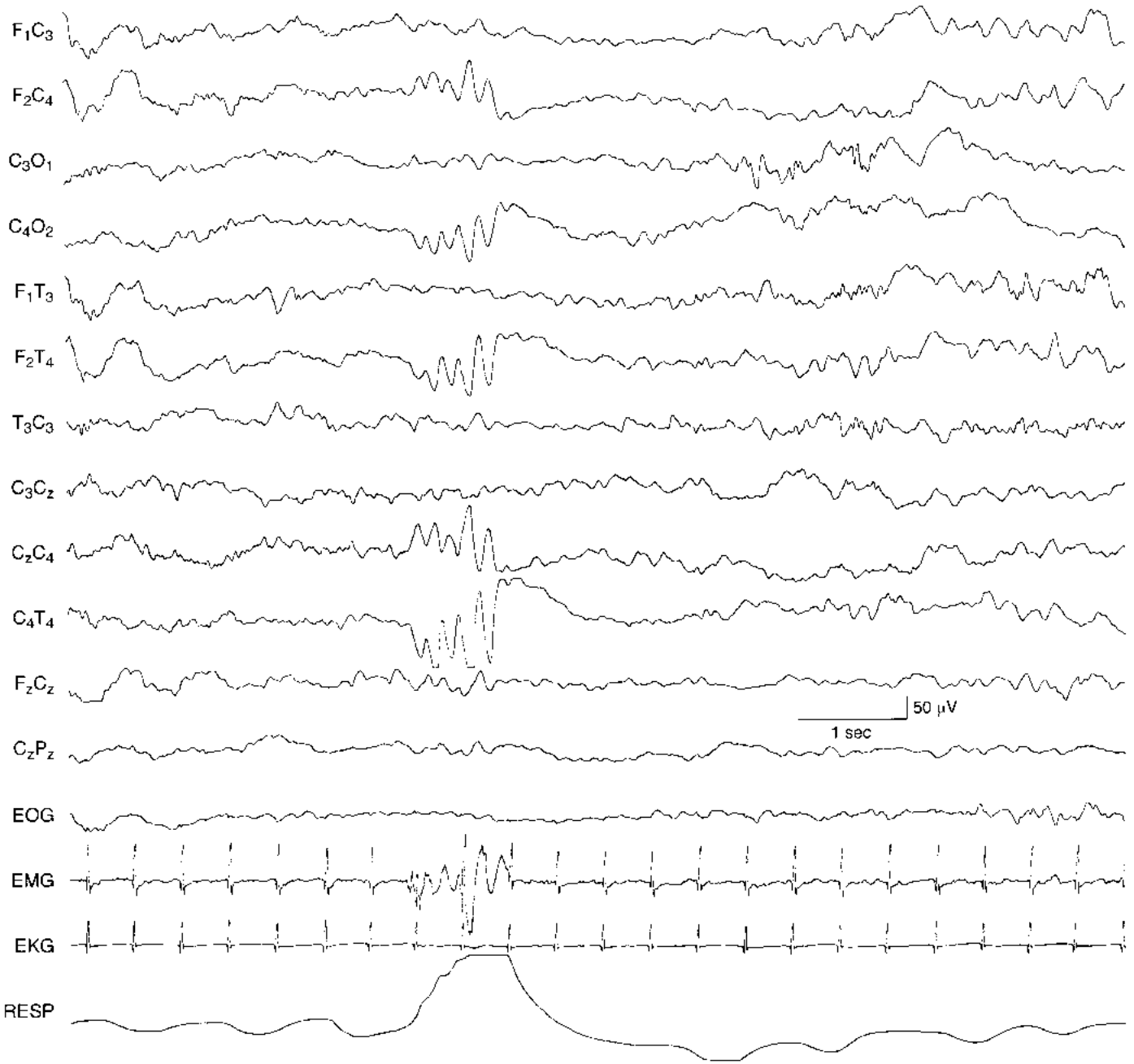

Figure 3.11 Moderately high amplitude, short duration, repetitive potentials due to head movement associated with sobbing. This infant experienced a brief sobbing episode characterized by shuddering that involved respiration and truncal muscles as well as the head, which was turned to the right. The rapid, rhythmic movement of the head resulted in brief rhythmic theta-like activity in the right central temporal region in this 40-week CA infant with normal background EEG activity. The simultaneous body movements are indicated by waveforms in the EMG channel.

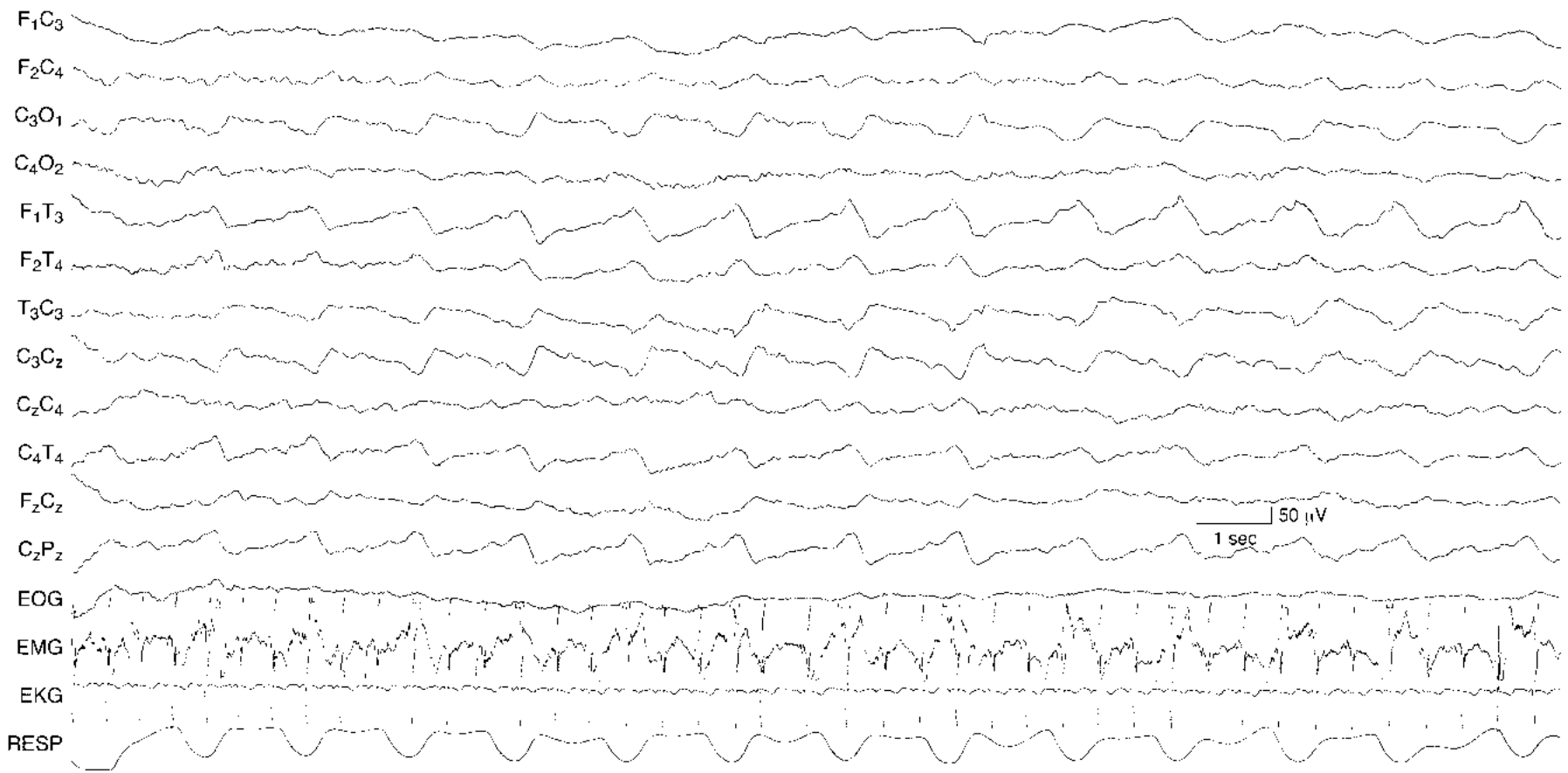

Figure 3.12 Slow periodic waves due to movements induced by mechanical ventilation. Mechanical ventilation may produce movements of the body and head, which in turn may result in EEG artifact such as in this recording with periodic, very slow waveforms that are not well lateralized and are aligned with deflections in the respiration channel. The background EEG in this 40-week CA infant is depressed and undifferentiated.

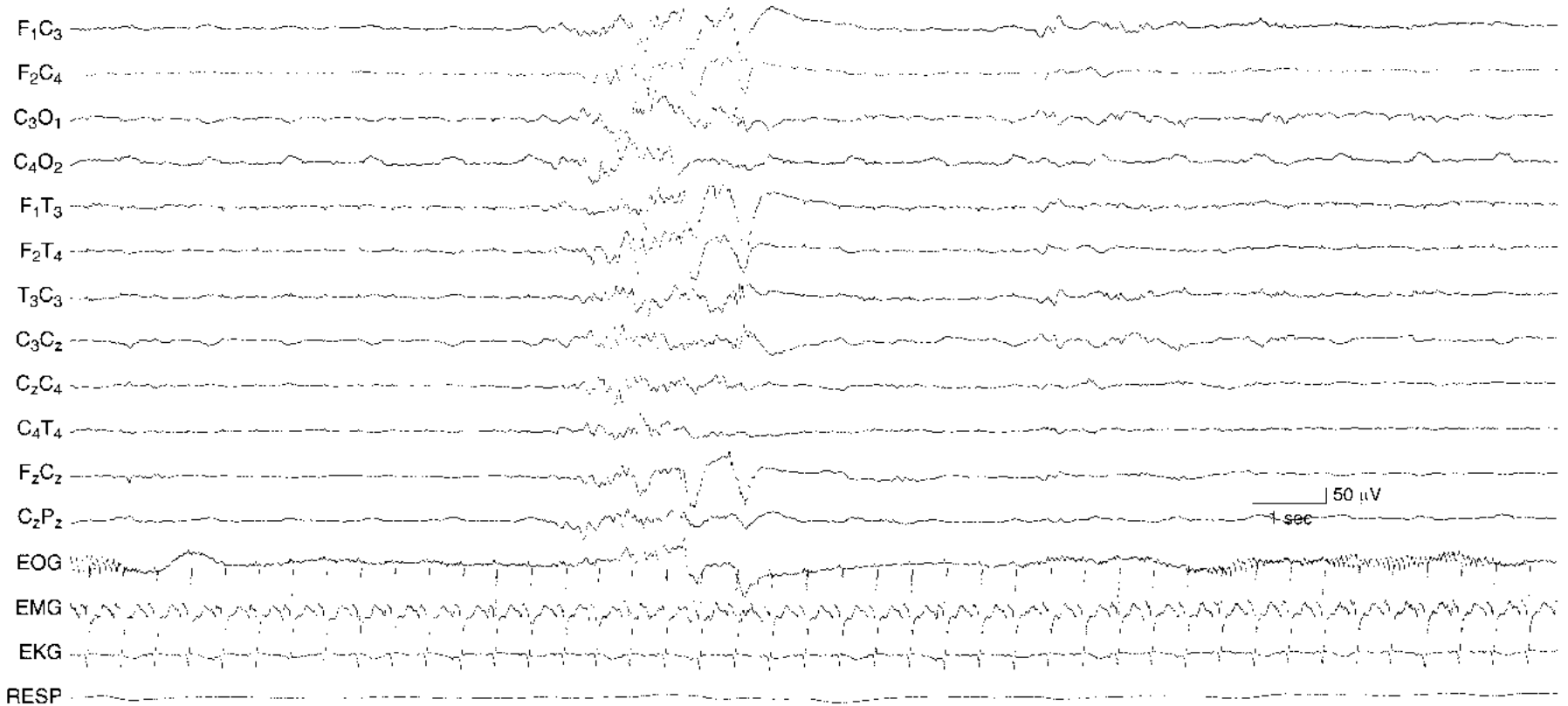

Figure 3.13 Periodic waves due to movement induced by ECMO pump. There are low voltage, periodic waves primarily in the right occipital and midline central regions that are associated with head movement induced by the action of the ECMO instrument used to support this 36-week CA infant. The background activity is characterized by a suppression-burst pattern.

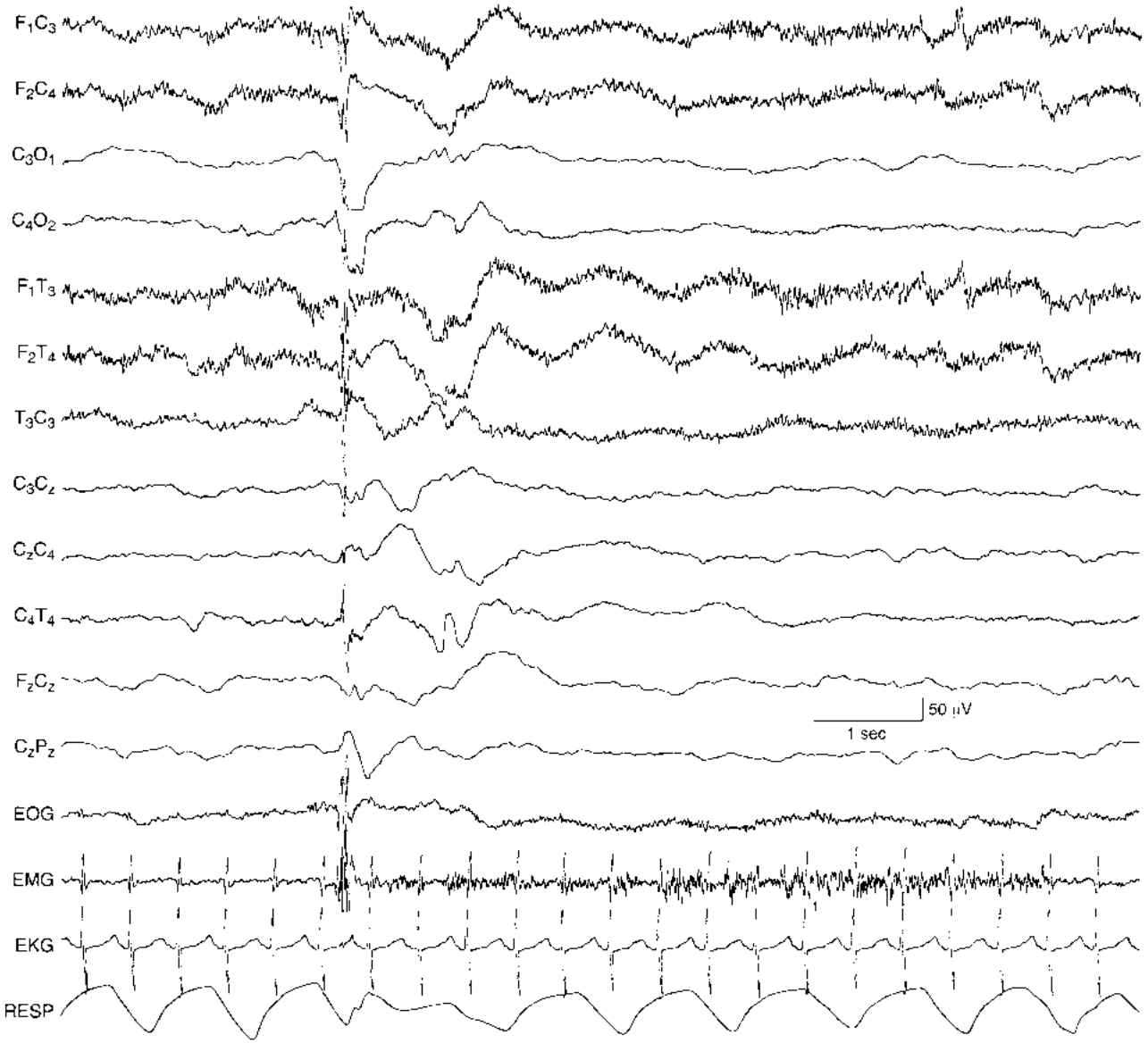

Figure 3.14 High amplitude generalized spike-like artifact associated with generalized myoclonic movement. A generalized myoclonic event in this 38-week CA infant resulted in a high amplitude generalized spike-like waveform. Movement is recorded as EMG that precedes the waveforms from scalp electrodes. There is sustained low voltage EMG in the anterior leads.

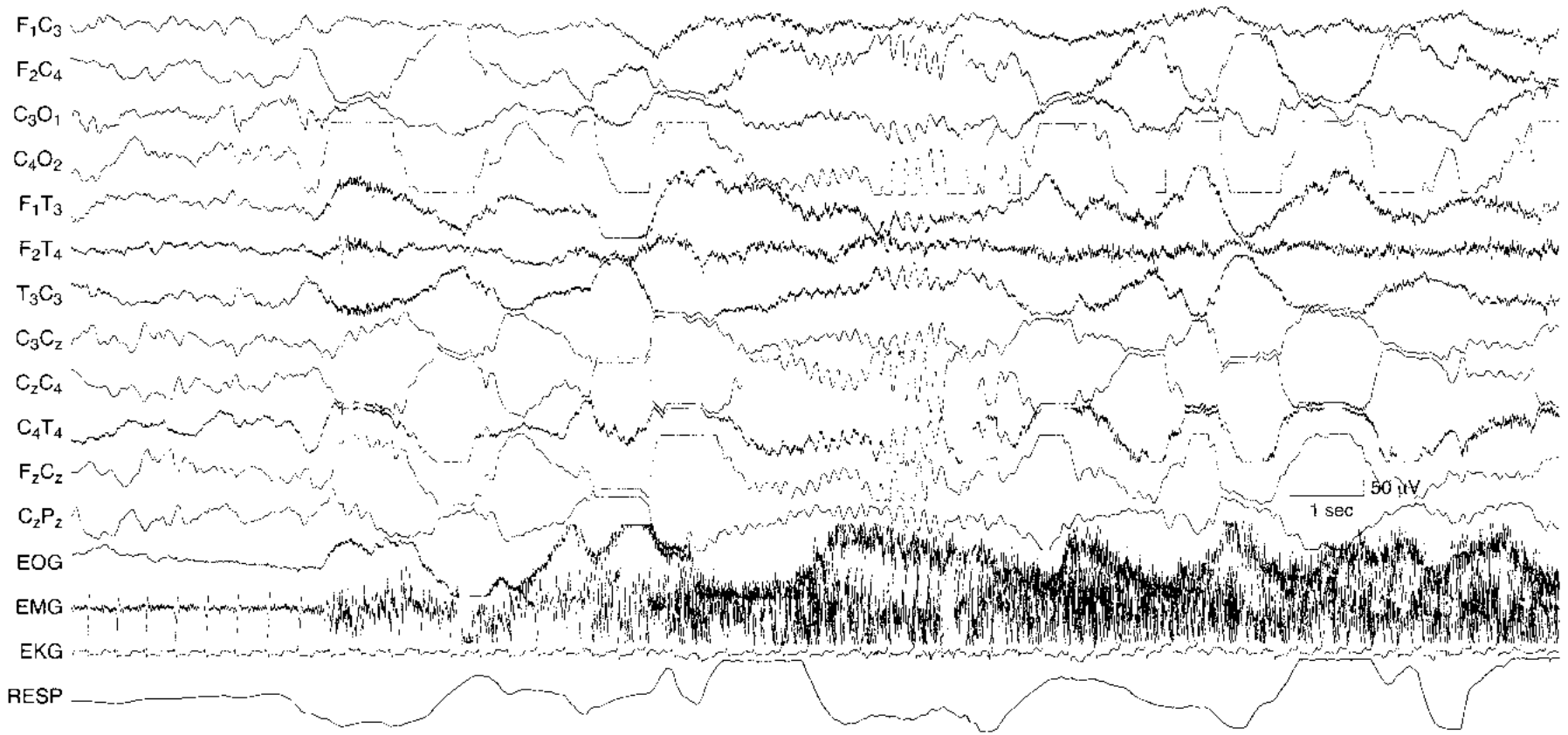

Figure 3.15 Rhythmic potentials due to tremors. High amplitude rhythmic theta activity is present with variable localization and is preceded and followed by high voltage, very slow activity. This is due to this 44-week CA infant's tremulousness or jitteriness. This activity was preceded and followed by slow random movements of the body. There is also sustained EMG activity that is superimposed upon the background EEG activity that is depressed and undifferentiated.

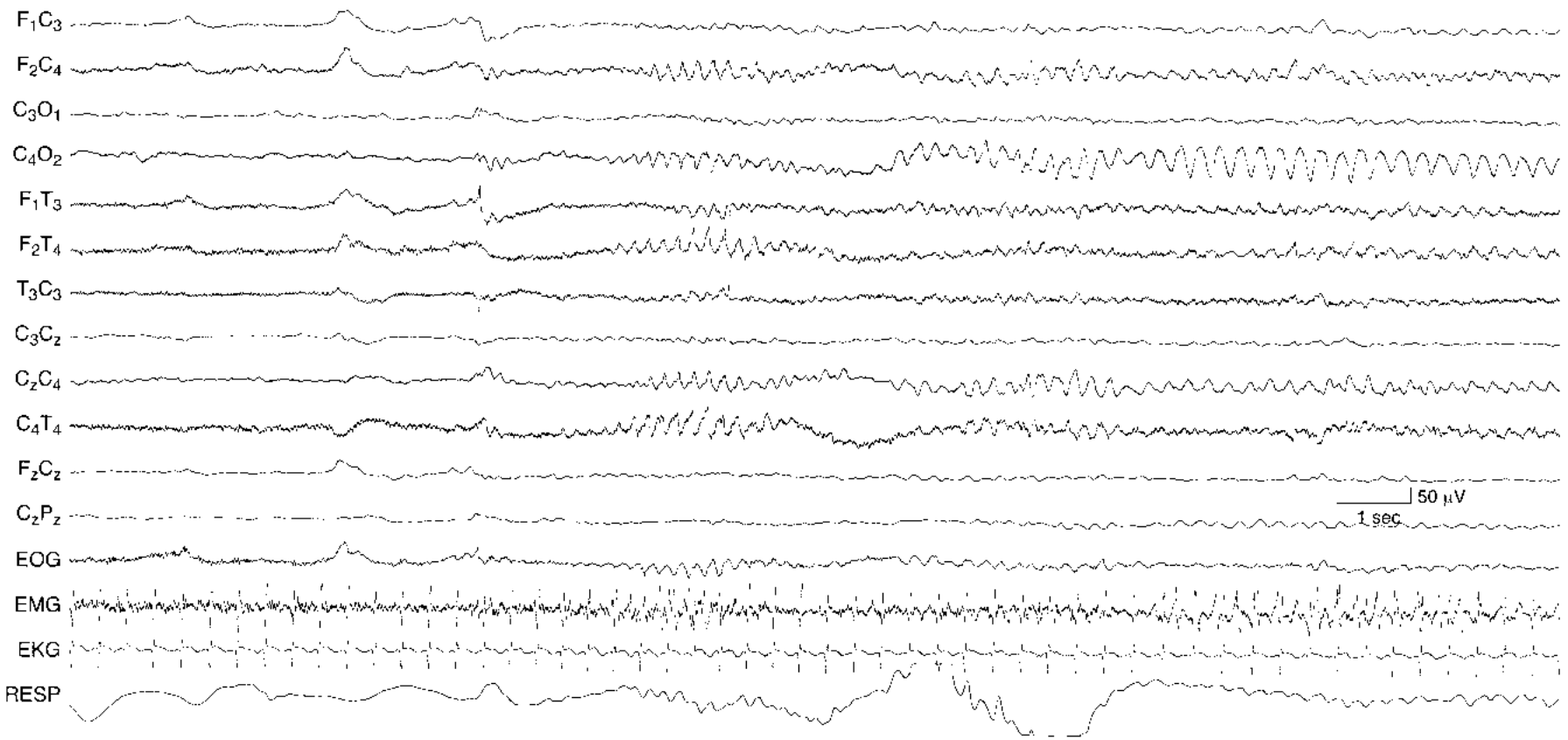

Figure 3.16 Rhythmic sharp potentials due to tremor. Rhythmic theta activity with a sharp morphology is present in the right central temporal region due to the tremors and jitteriness of this 40-week CA infant. There is also low voltage EMG primarily in temporal regions.

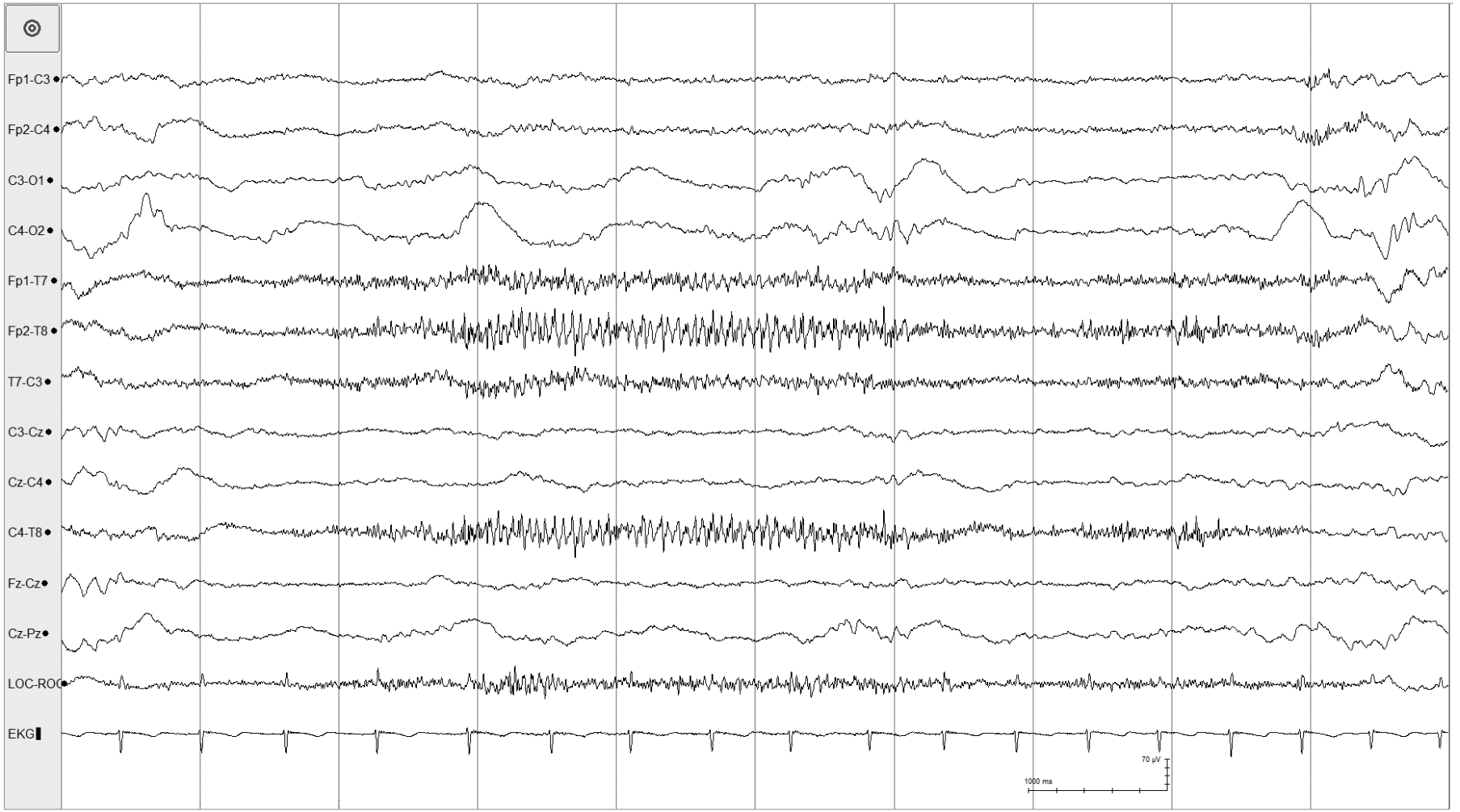

Figure 3.17 Rhythmic sharp waves associated with jitteriness. A buildup of rhythmic fast sharp waves are present in the temporal regions bilaterally but more prominently on the right in this 38-week CA infant with a normal background.

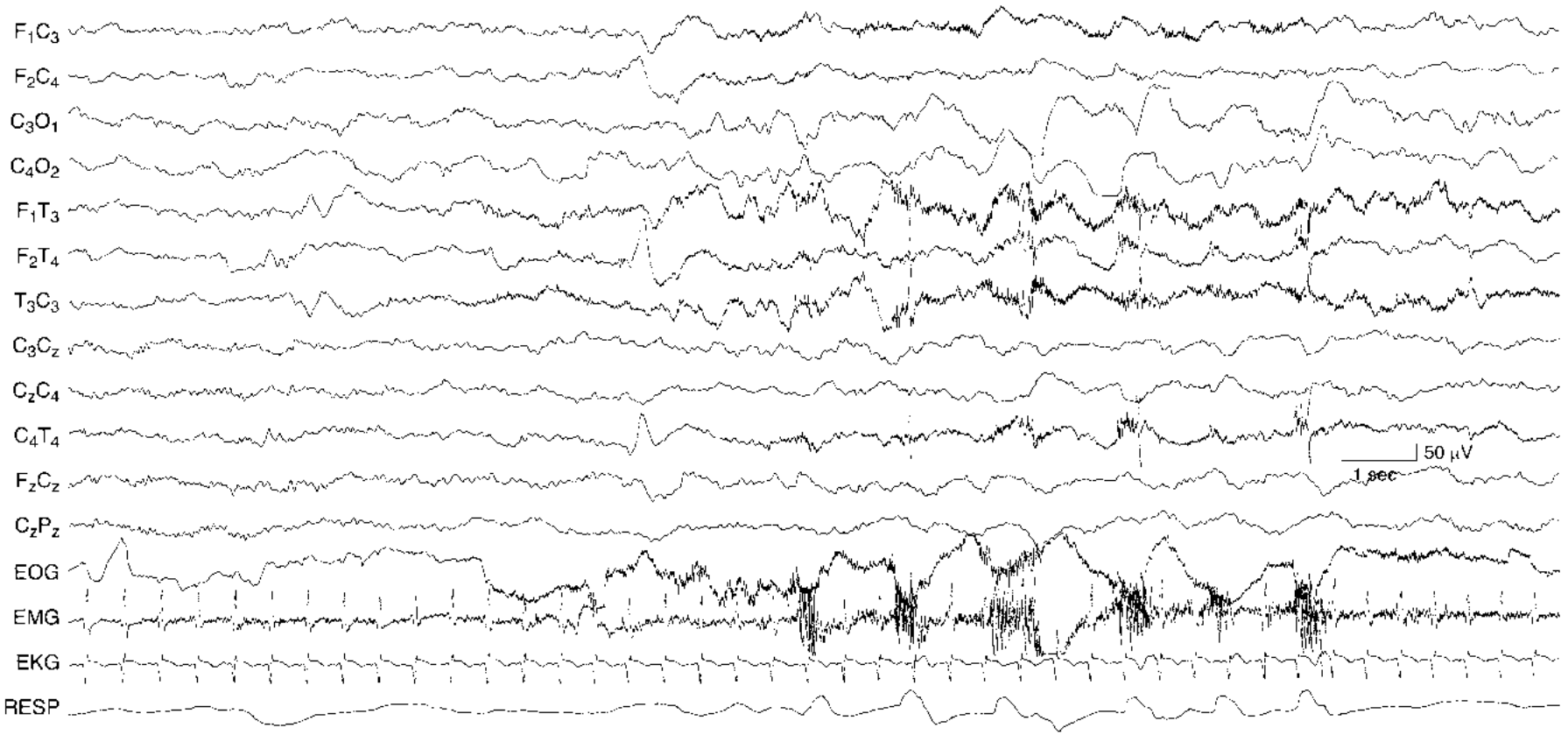

Figure 3.18 Rhythmic slow activity due to sneezing. High voltage, rhythmic slow activity is present in the left and right temporal regions associated with repetitive sneezing or coughing of this 39-week CA infant with normal EEG background activity. There is also superimposed EMG activity in the EEG channels and movement is also suggested by activity in the EMG channel.

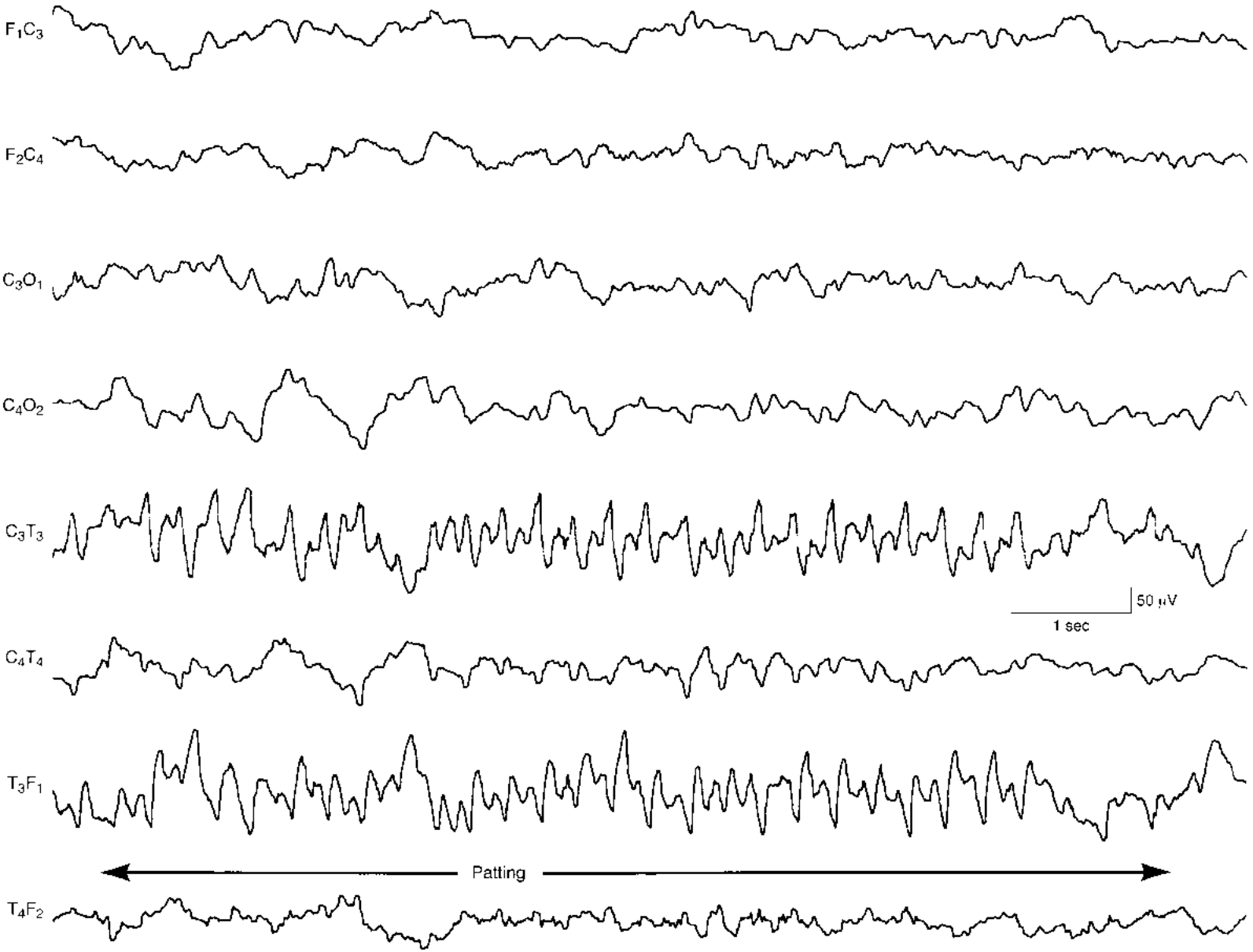

Figure 3.19 Rhythmic polymorphic activity induced by patting. Polymorphic rhythmic activity is present in the left temporal region that is induced by patting or comforting this 40-week CA infant with a normal background EEG.

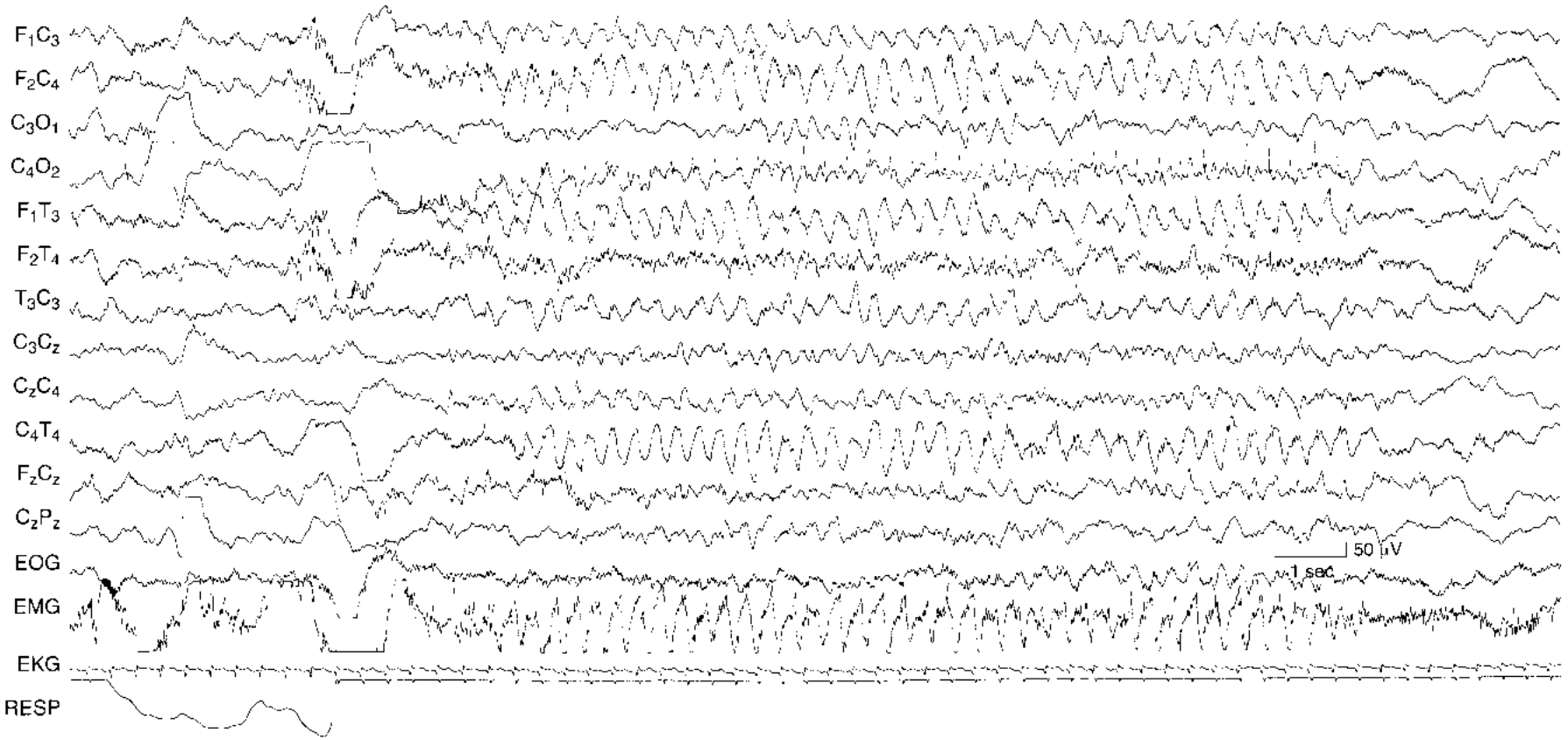

Figure 3.20 Rhythmic slow activity induced by patting. High voltage, rhythmic, monomorphic, delta-like activity is induced by patting this 40-week CA infant with normal EEG background activity.

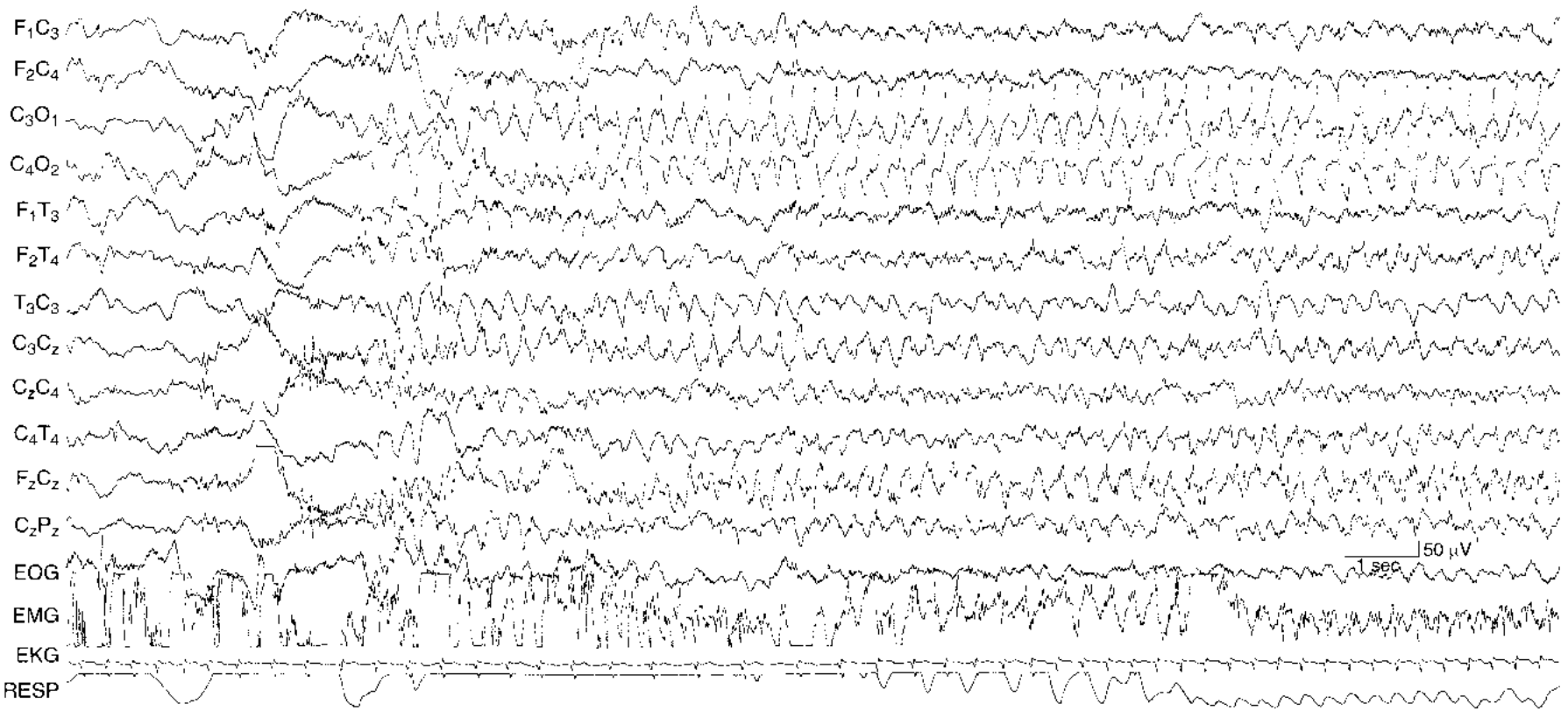

Figure 3.21 Rhythmic sharp wave activity induced by patting. An apparent build-up of rhythmic sharp waves is present in the occipital regions bilaterally with some lateralization to leads on the left associated with patting of this 40-week CA infant. The background EEG activity is normal.

Figure 3.22 Rhythmic polymorphic activity induced by burping. Abrupt onset of rhythmic spike and slow wave activity is present in the right and left parietal regions with expression at lower voltage in other regions. This activity was induced by burping in this 41-week CA infant with normal background EEG.

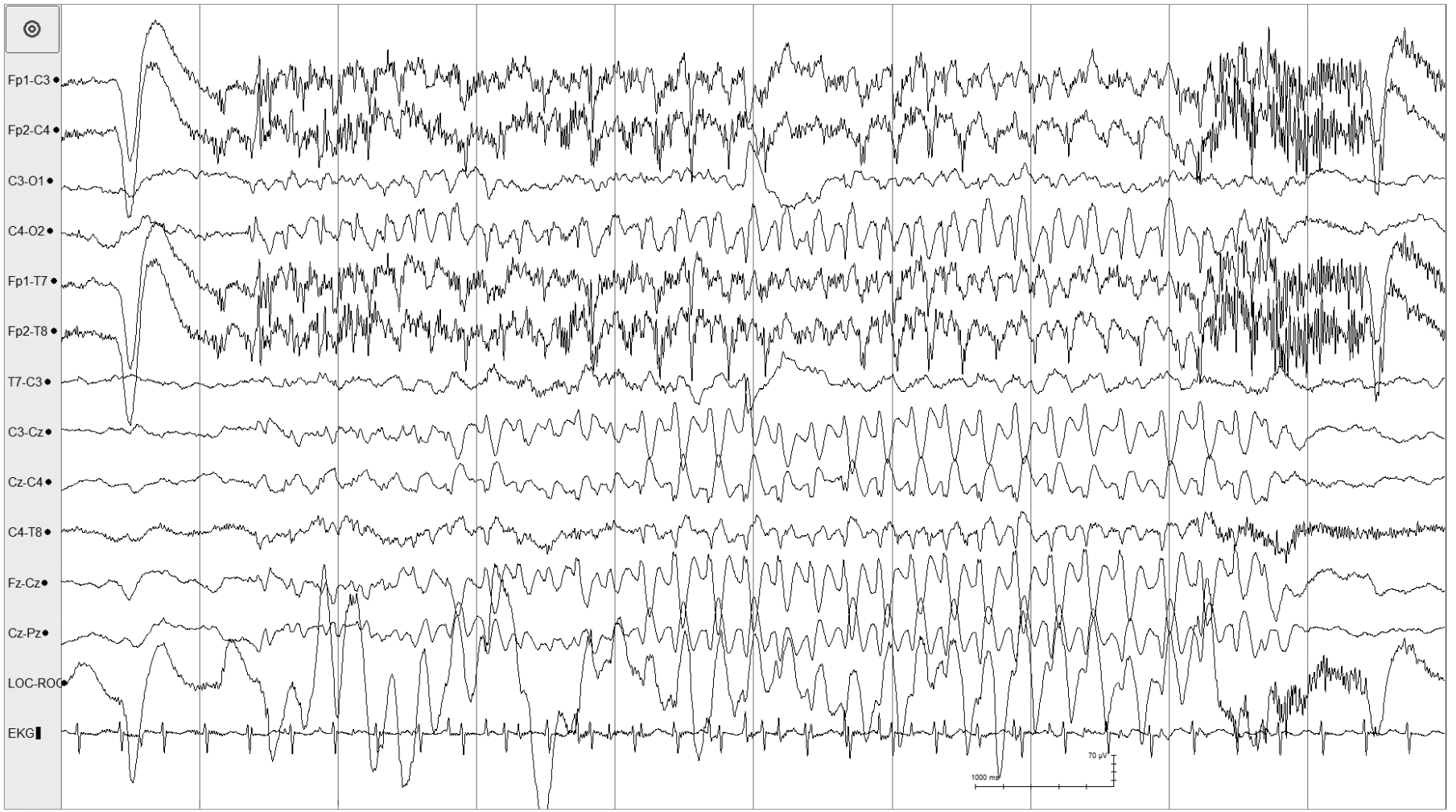

Figure 3.23 Rhythmic polymorphic activity induced by burping. There is abrupt onset and resolution of rhythmic spike and sharp and slow wave activity in this 41-week CA infant with a normal background EEG. Discharges initially appear on the right, then independently in the midline central region with sudden resolution on all regions.

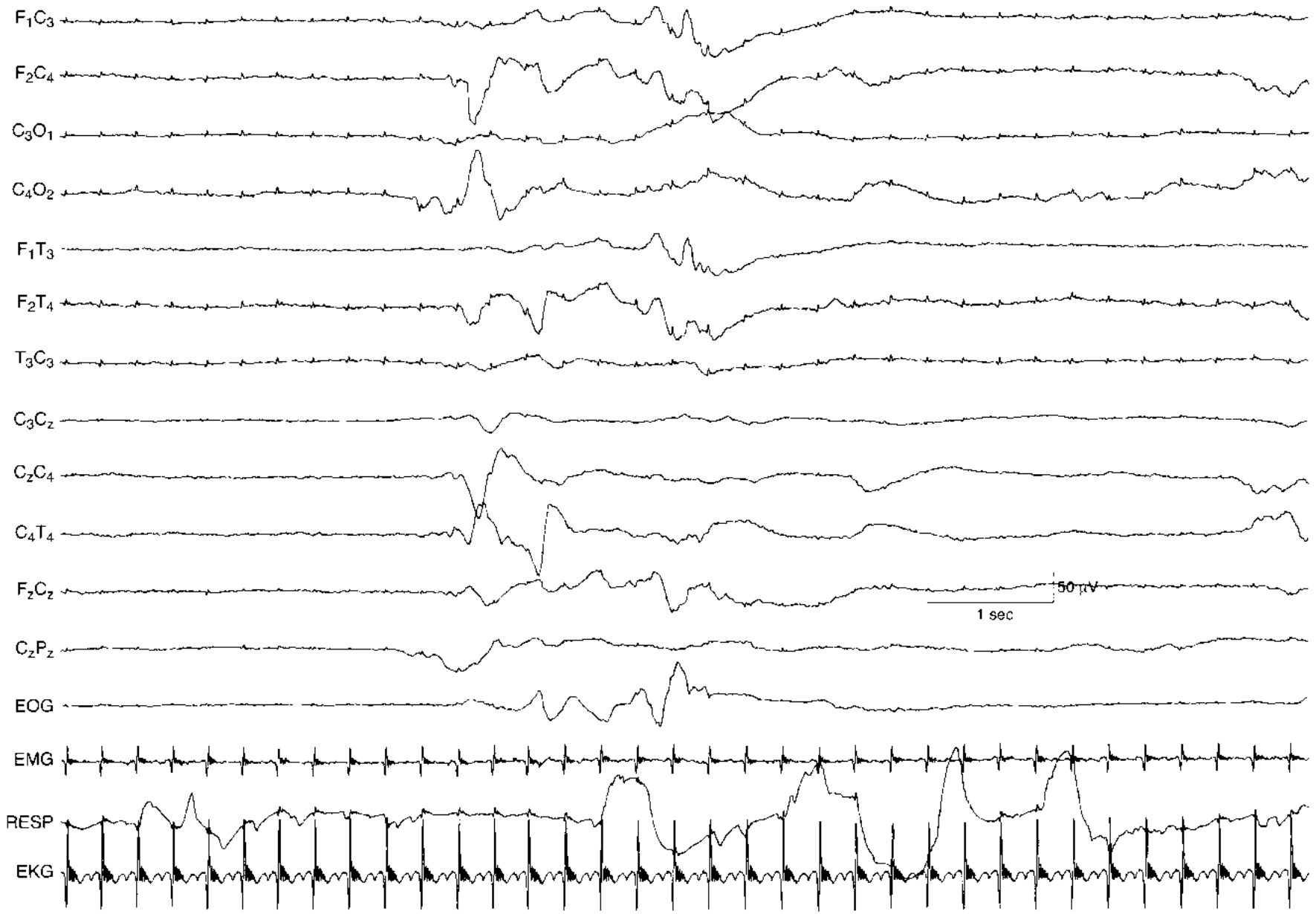

Figure 3.24 Electrocardiogram (EKG). The EKG is present in several channels in this 39-week CA infant with suppression-burst EEG background activity.

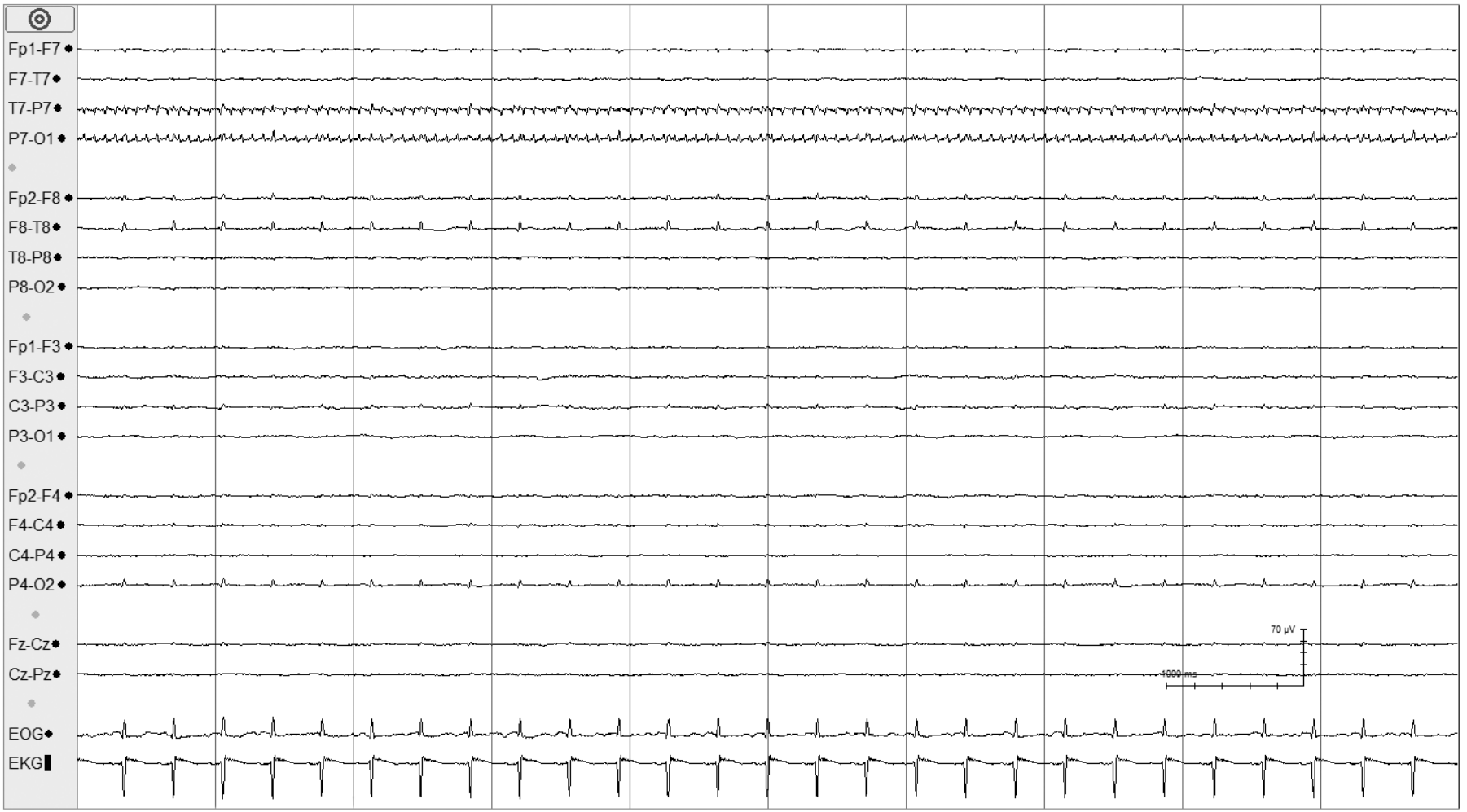

Figure 3.25 EKG and sustained EMG. Low voltage rhythmic sharp waves due to EMG are present in the left parietal region and there is independent EKG artifact present in anterior and posterior electrodes on the right in this 39-week CA infant with hypoxic ischemic encephalopathy. The background EEG is depressed and undifferiented.

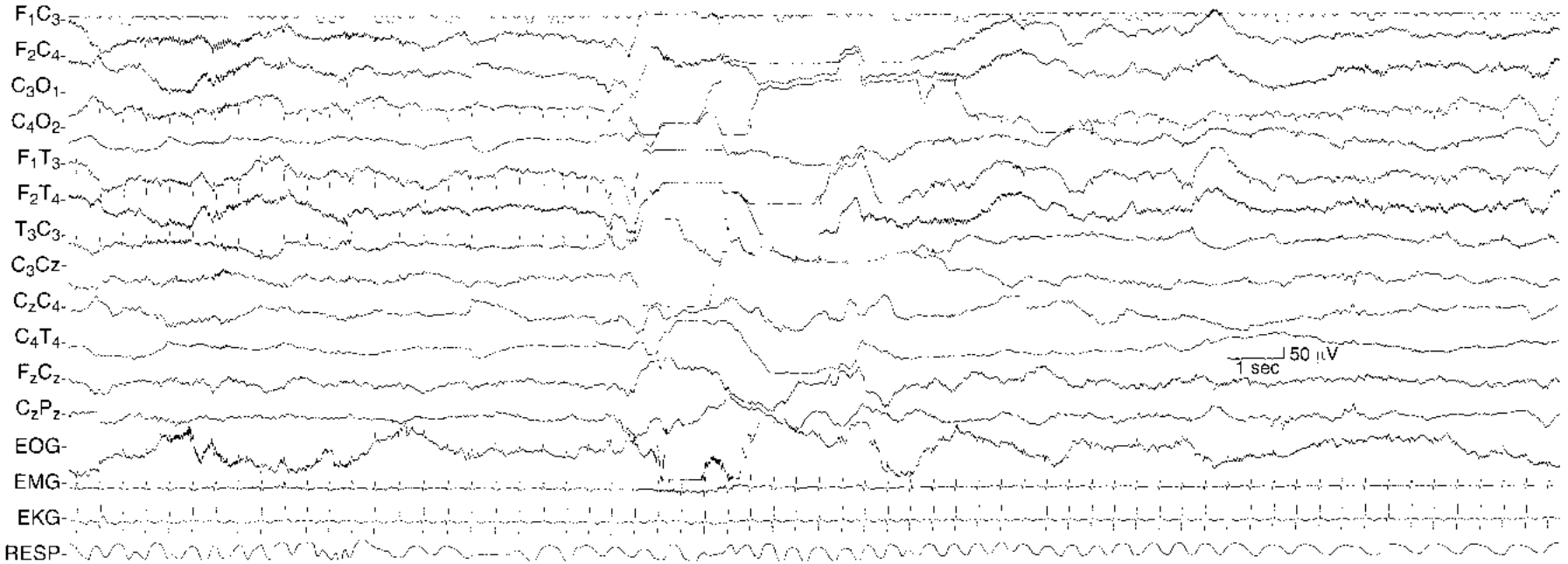

Figure 3.26 EKG altered with change in head position. The EKG is present more prominently in the early portion of this recording with high amplitude spike-like activity in leads from the left temporal and occipital regions. The amplitude of the waves is reduced and they are less prominent in the temporal region when the infant's head is moved to the midline by the ENDT. This movement is marked by generalized high-amplitude slow activity in the middle of this segment. The infant is 40-weeks CA and the background EEG activity is depressed and undifferentiated.

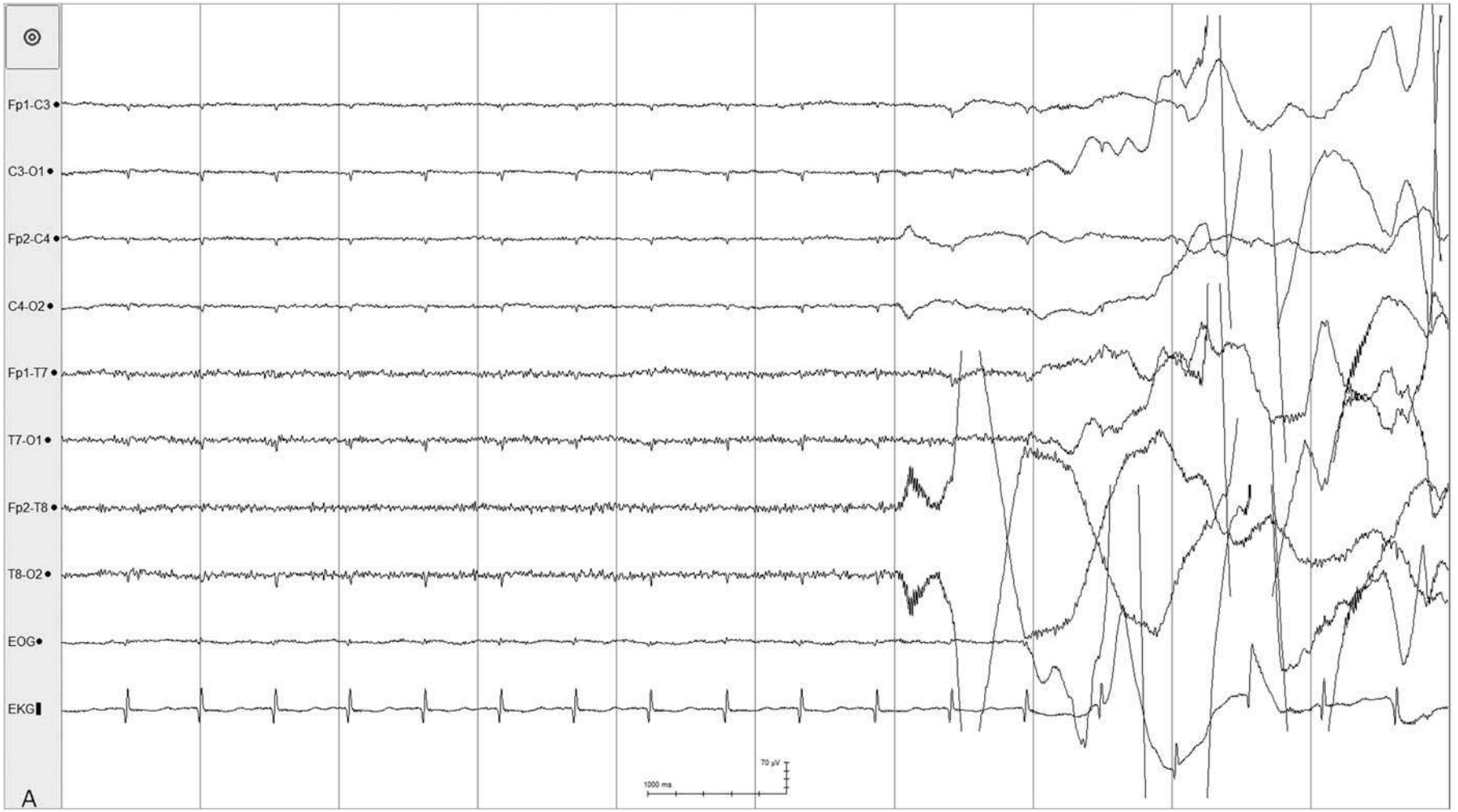

Figure 3.27 (A) and (B) EKG artifact attenuated with change in head position. (A) Recurrent EKG artifact is present in various electrodes, although most prominent on the left. At the end of the sample there is myogenic and movement potential due to repositioning of the infant's head. (*continued)*

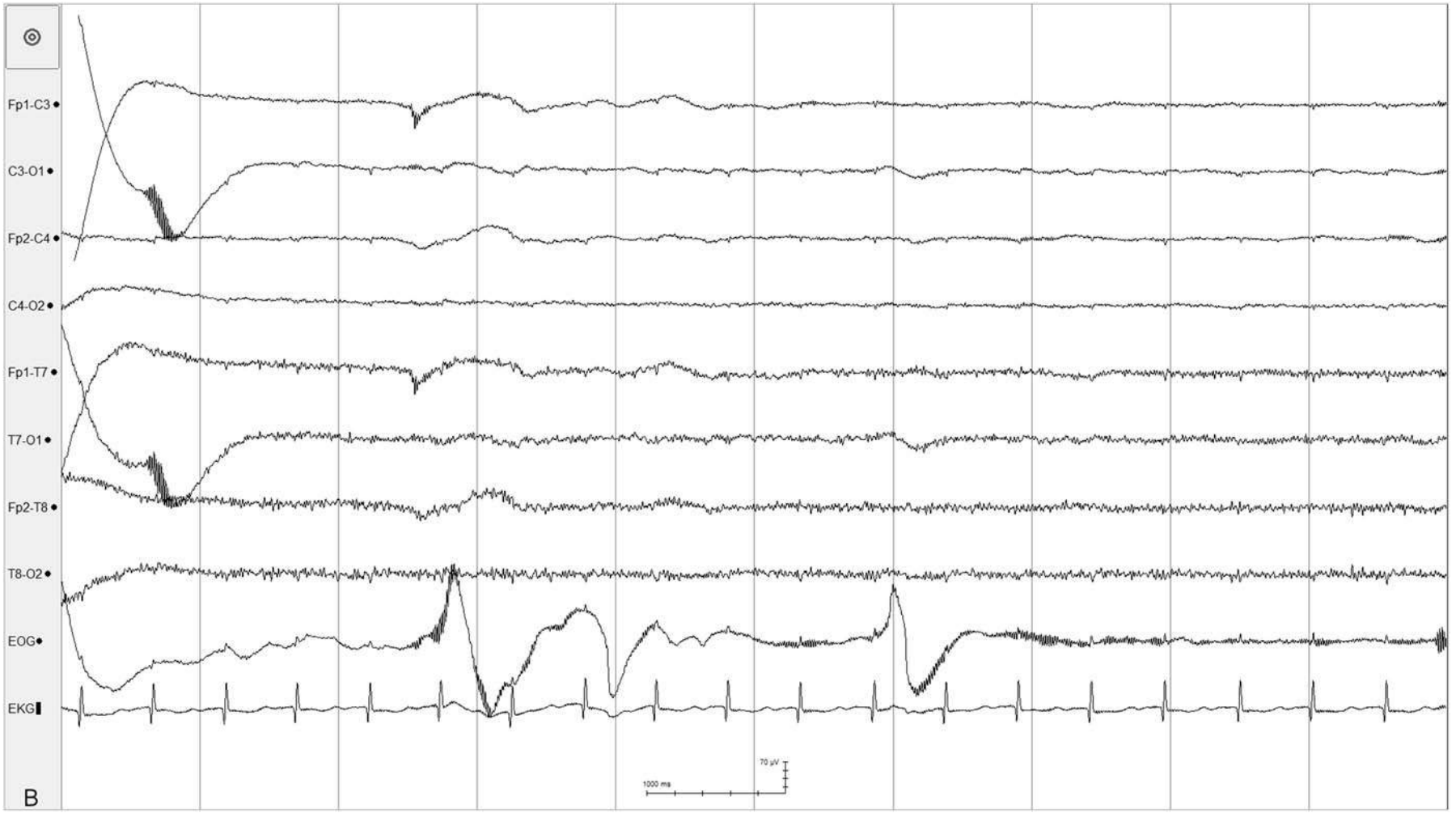

Figure 3.27 (*continued*) **(B)** This sample is a continuous recording from **(A)**, with the initial portion of this sample consisting of the sample myogenic and movement potential due to repositioning of the infant's head. This repositioning resulted in a significant attenuation of the EKG artifact in the recording. This occurred in a 39-week CA infant with hypoxic ischemic encephalopathy and with a depressed and undifferentiated background EEG.

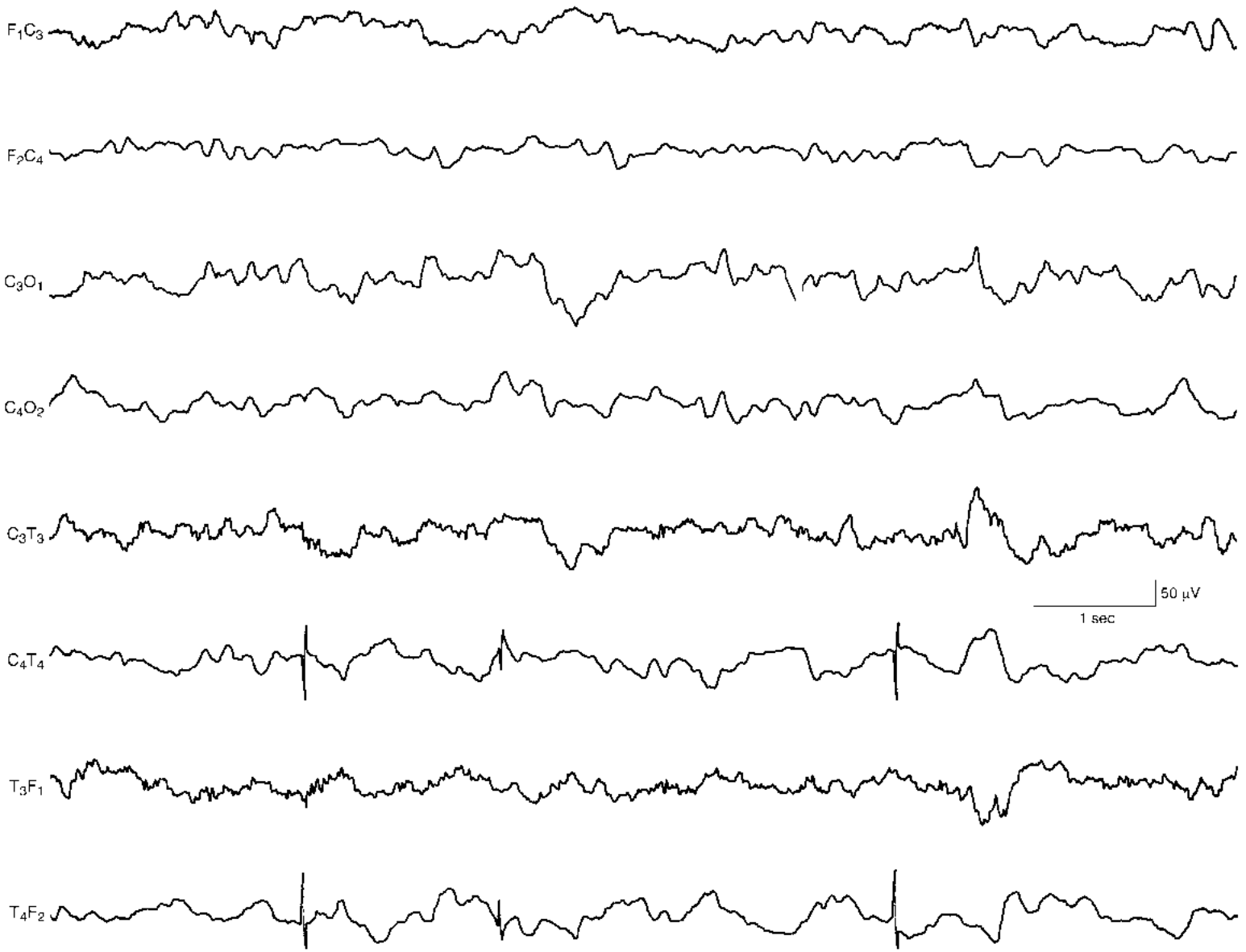

Figure 3.28 Isolated, focal EMG potential due to sucking. There are isolated EMG potentials in the right temporal region due to sucking motions of this 40-week CA infant. The background EEG is within the range of normal variation.

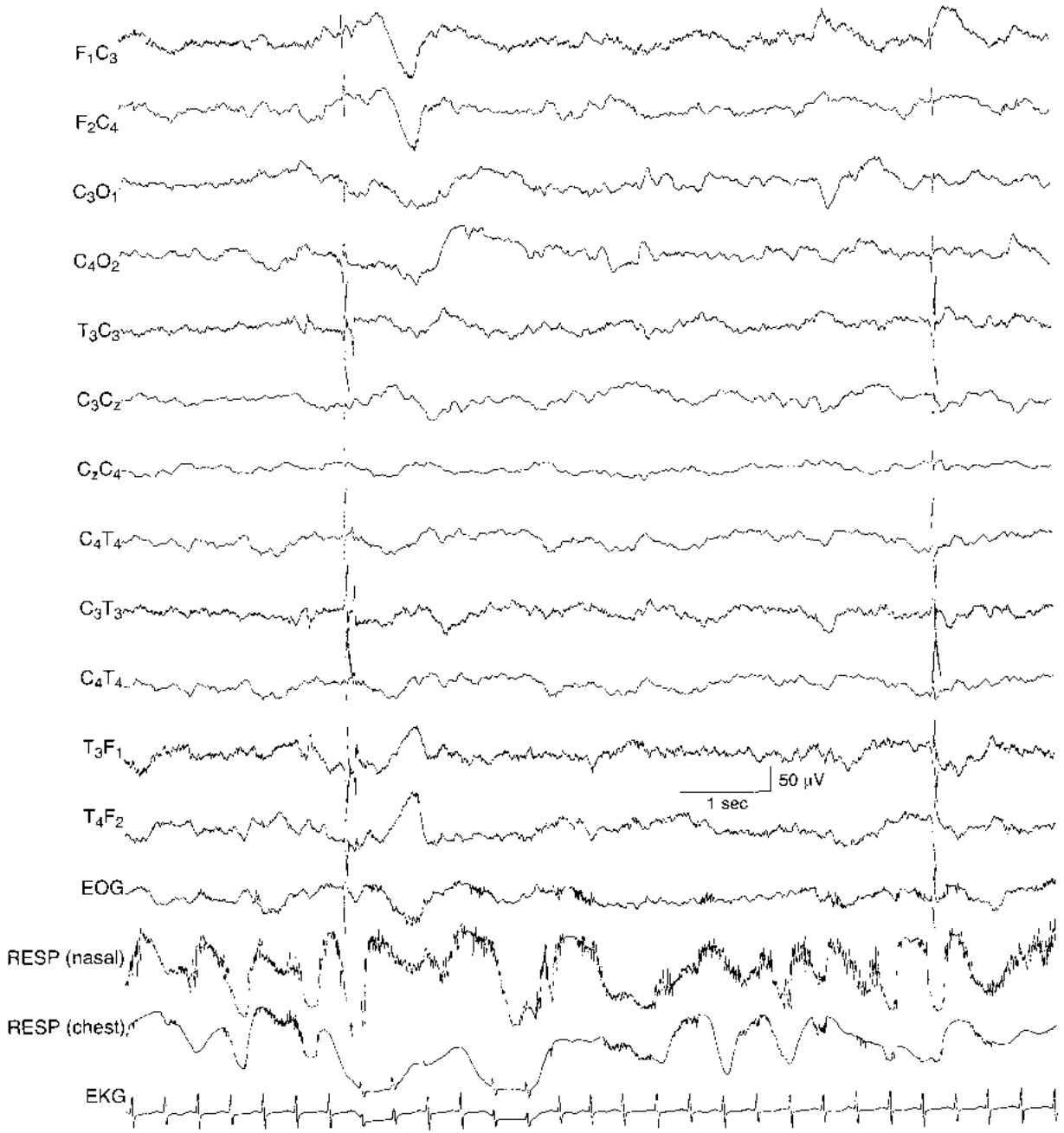

Figure 3.29 Wide reflection of EMG potentials due to sucking. The EMG due to sucking arises from the left and right temporal regions but has variable amplitude and a wide reflection on the two sides in this 40-week CA infant with normal EEG background activity.

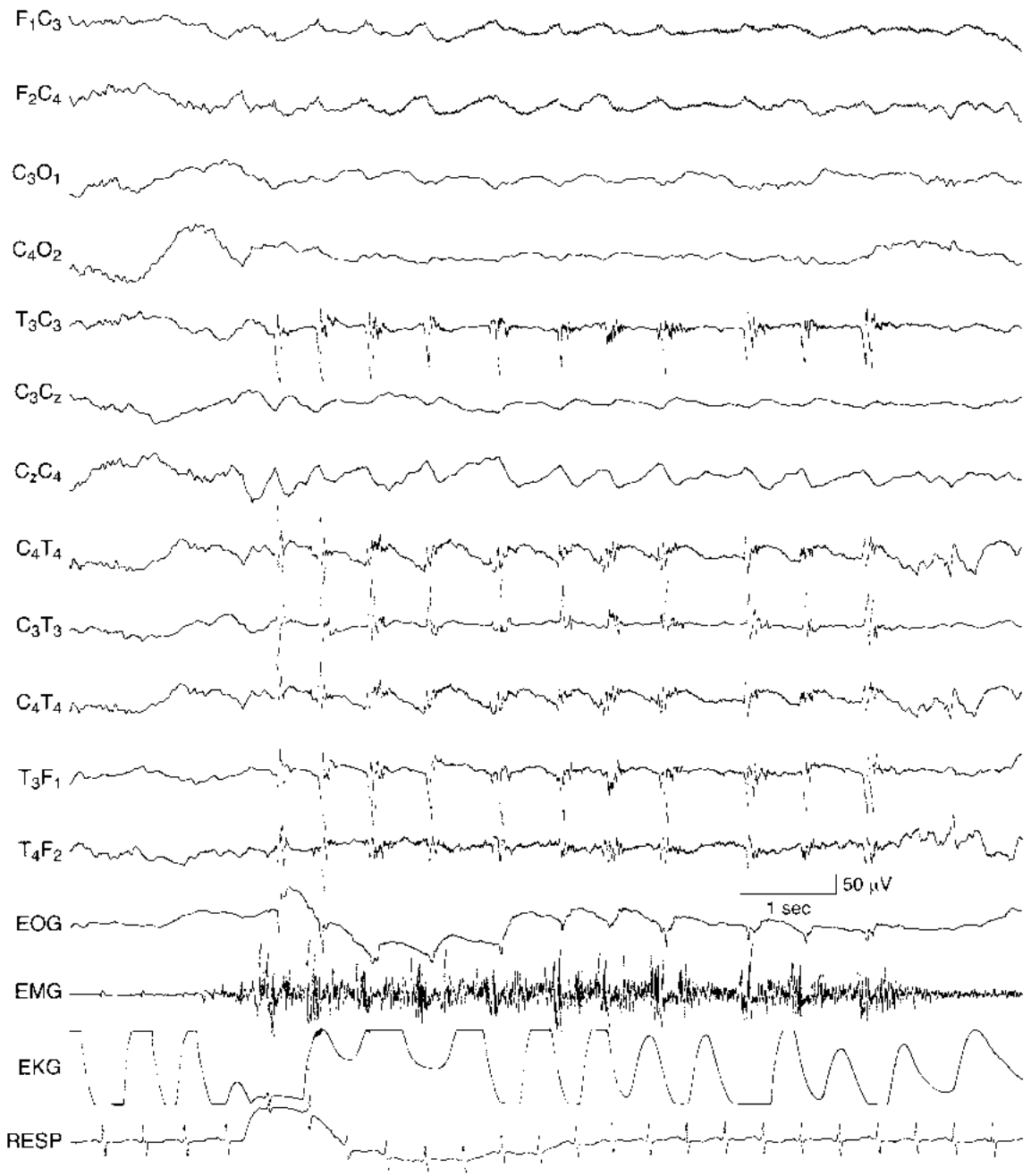

Figure 3.30 Periodic EMG potentials due to sucking. This EMG activity due to sucking has a complex morphology. It is periodic, primarily in the left temporal region. There is normal EEG background activity in this 40-week CA infant.

Figure 3.31 Periodic bursts of EMG potentials due to sucking. Brief bursts of repetitive EMG potentials occur periodically in the temporal regions bilaterally in this 41-week CA infant with normal EEG background activity. Low voltage sustained EMG is present in anterior leads.

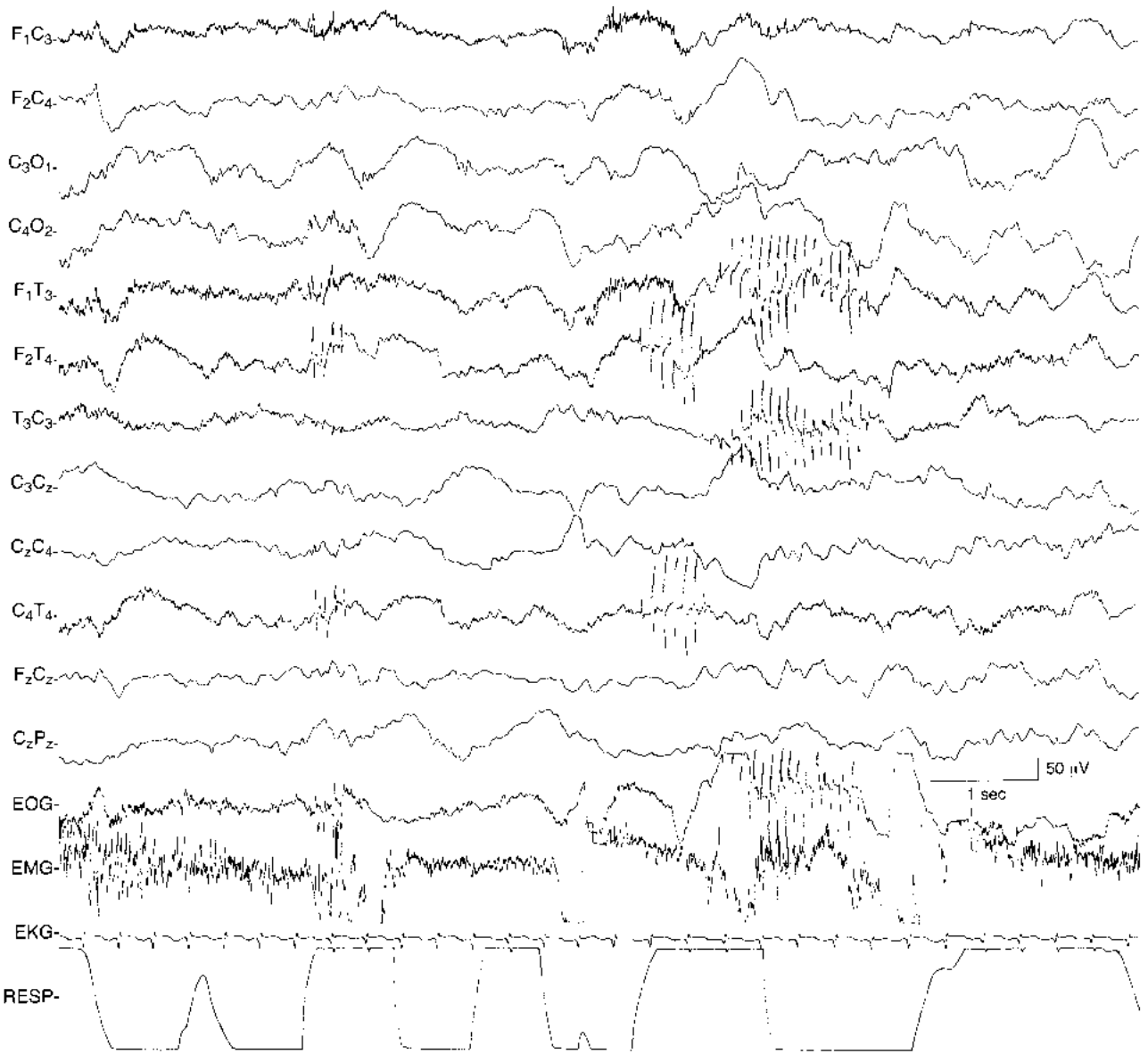

Figure 3.32 Multifocal, repetitive EMG potentials due to jaw tremor. Bursts of repetitive EMG due to tremulousness of the jaw are present independently in the left and right temporal regions in this 42-week CA infant with normal EEG background activity.

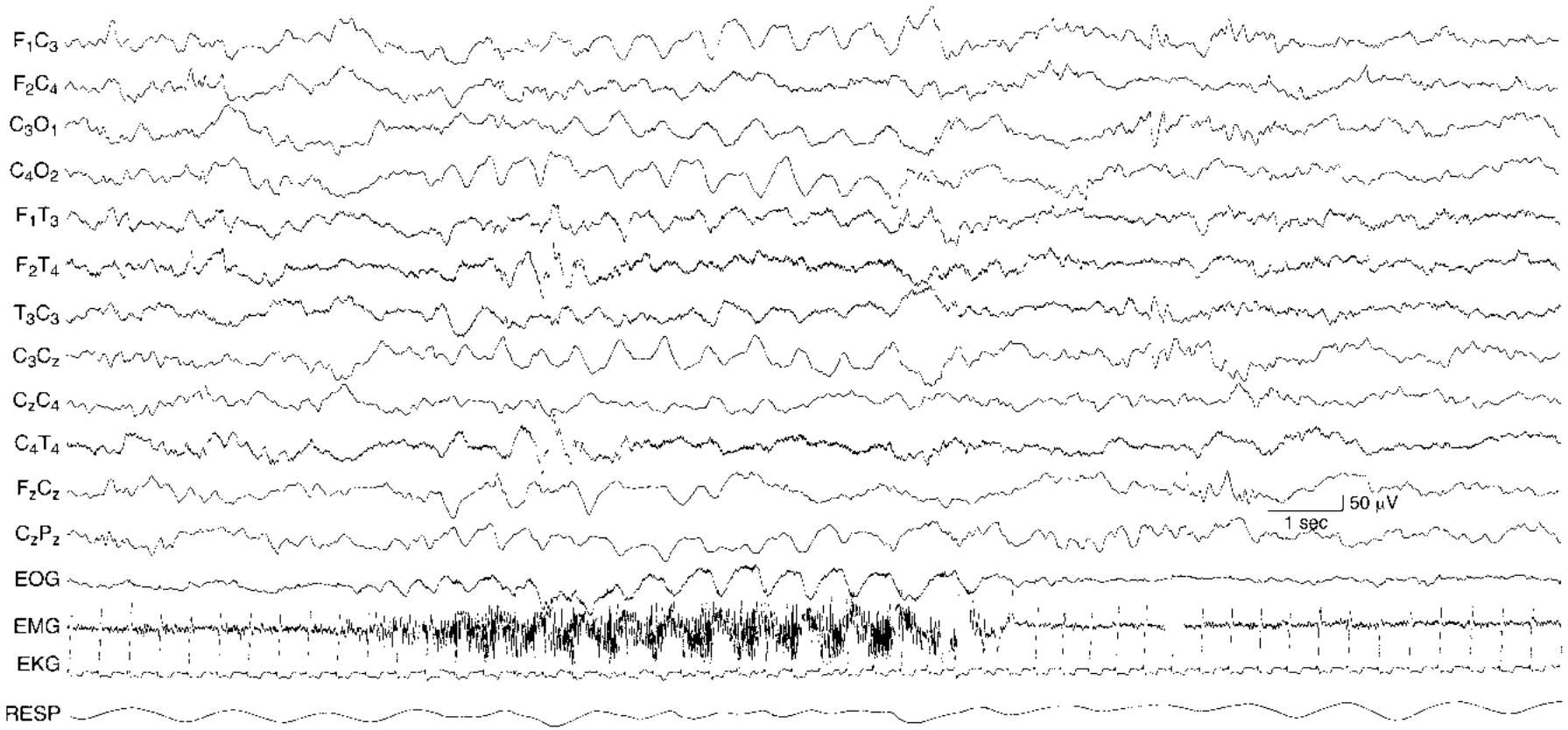

Figure 3.33 Rhythmic slow activity and EMG associated with sucking. Rhythmic slow activity is associated with sucking in this 43-week CA infant. Although associated with sucking, this activity is not produced by endogenous potentials, but rather by movement of the head that occurs in conjunction with vigorous sucking. The background EEG activity is within the range of normal variation. The EMG channel reflects increased activity associated with sucking.

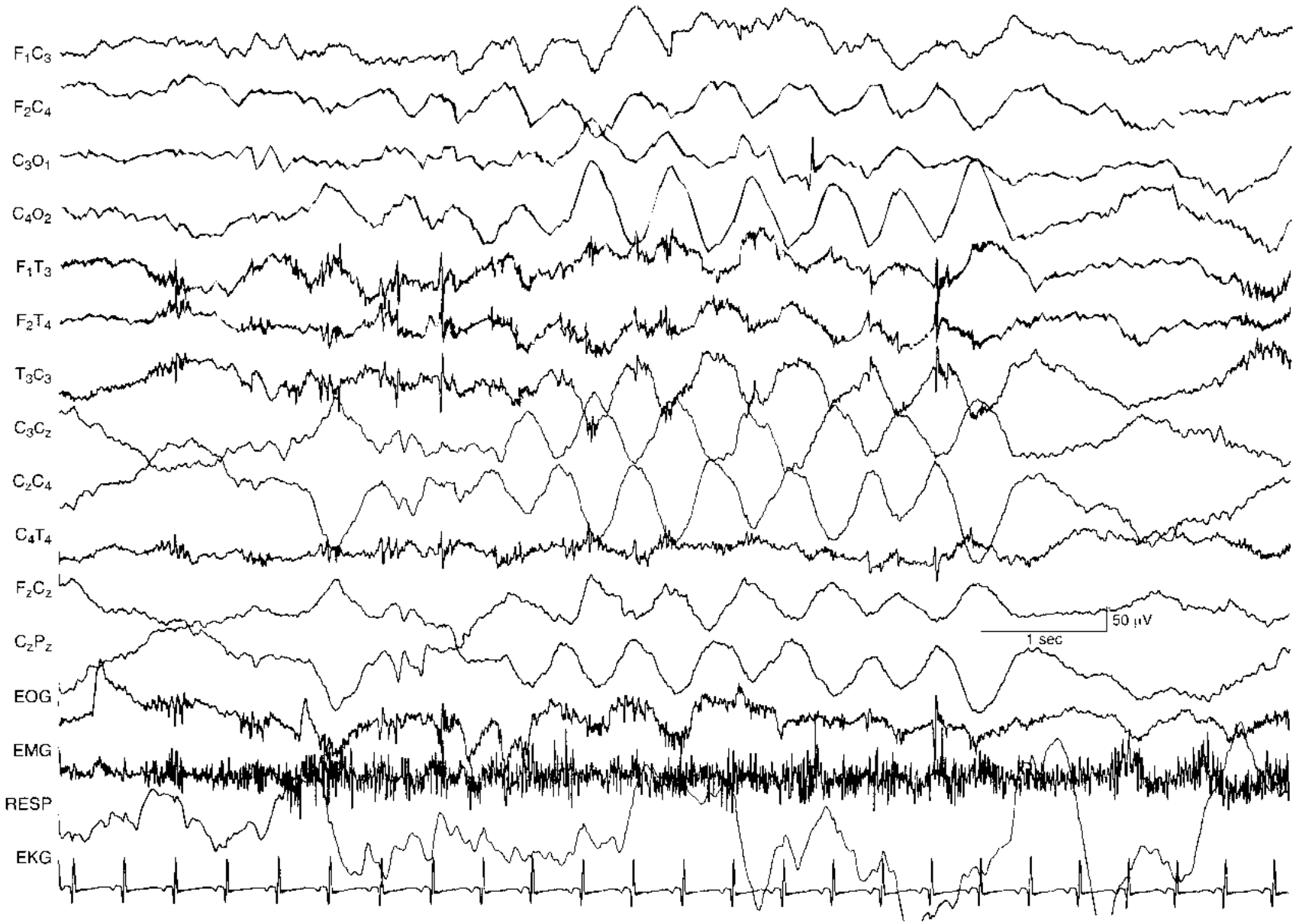

Figure 3.34 Rhythmic slow activity associated with sucking. There are rhythmic EMG potentials in the temporal regions and rhythmic slow activity induced by head movement in the right and midline central regions associated with sucking in this 40-week CA infant with normal EEG background activity.

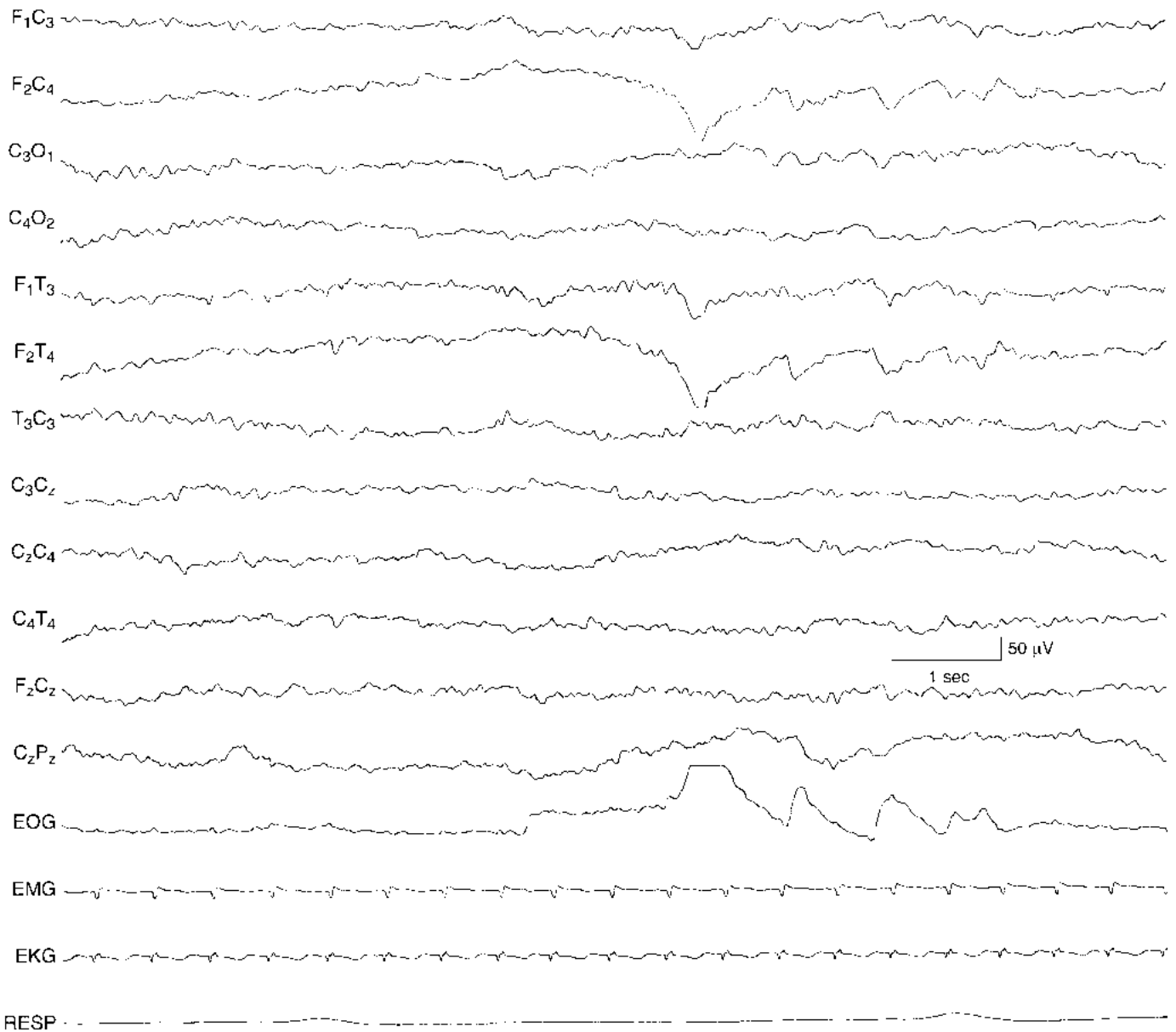

Figure 3.35 Slow activity due to eye movements. Eye movement is reflected in the right frontal region appearing as a brief run of slow activity that aligns with the activity recorded on the EOG channel. The infant is 40-weeks CA with normal EEG background activity.

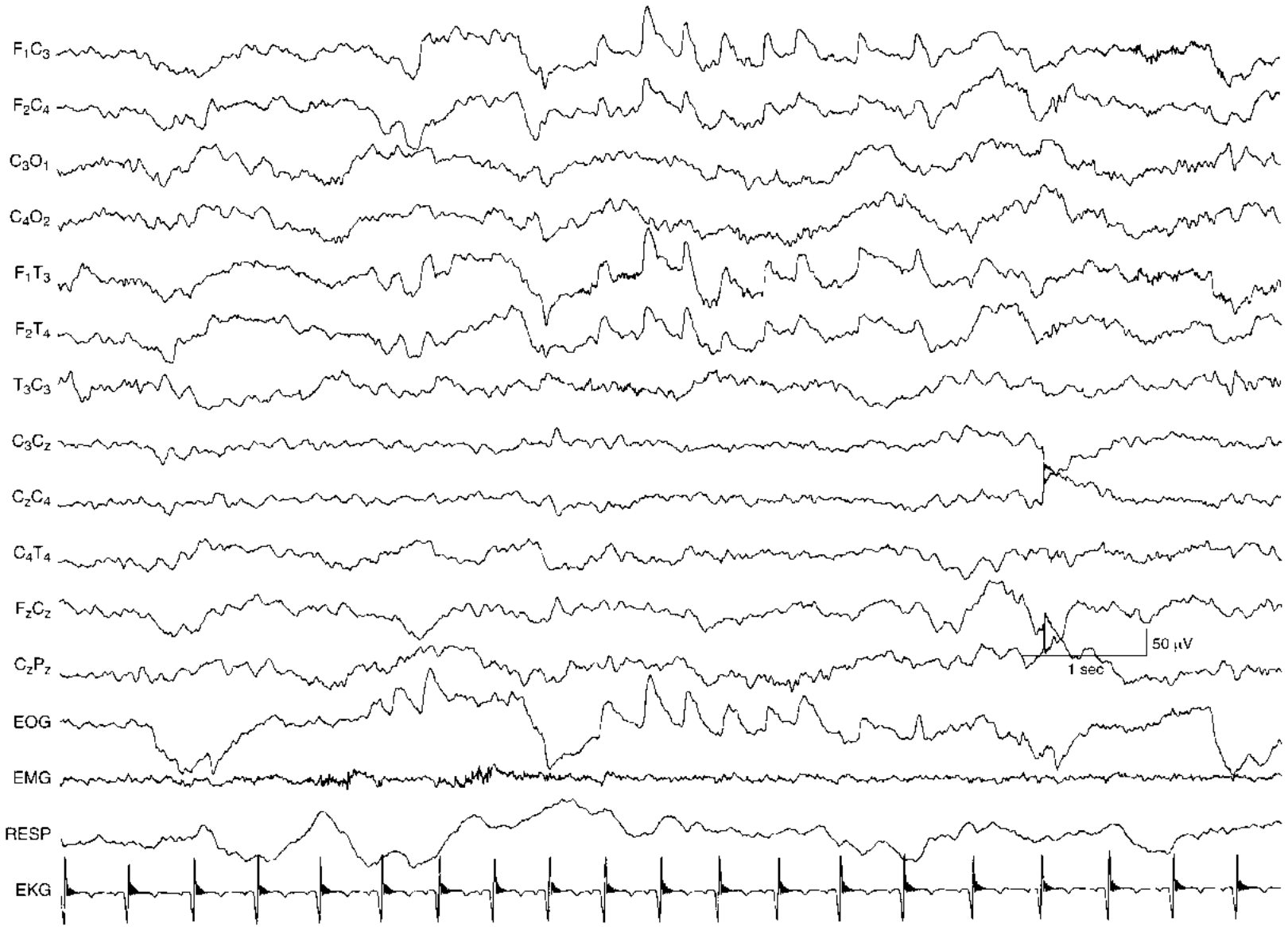

Figure 3.36 Intermittent sharp activity due to eye movements. Rhythmic, slow, sharp waves are present in the frontal regions bilaterally, higher in amplitude on the left, aligned with the recorded EOG and occurring in association with clinically observed nystagmus. The infant is at 40-weeks CA with normal EEG background activity.

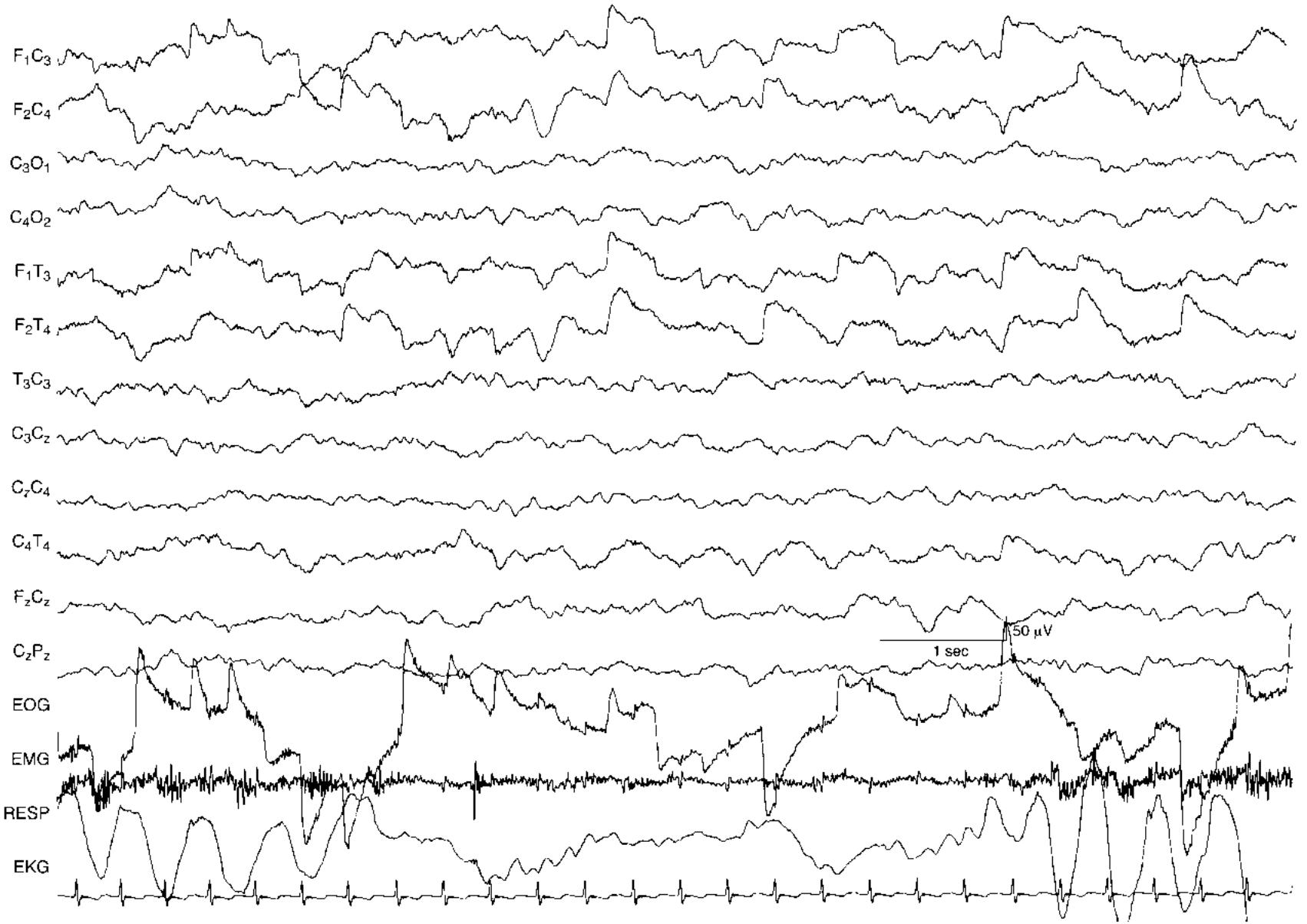

Figure 3.37 Semirhythmic slow activity due to eye movements. Slow, semirhythmic activity, with a variable geometric morphology is present in the frontal regions associated with eye movements that are also represented in the EOG channel in this 40-week CA infant with normal EEG background activity.

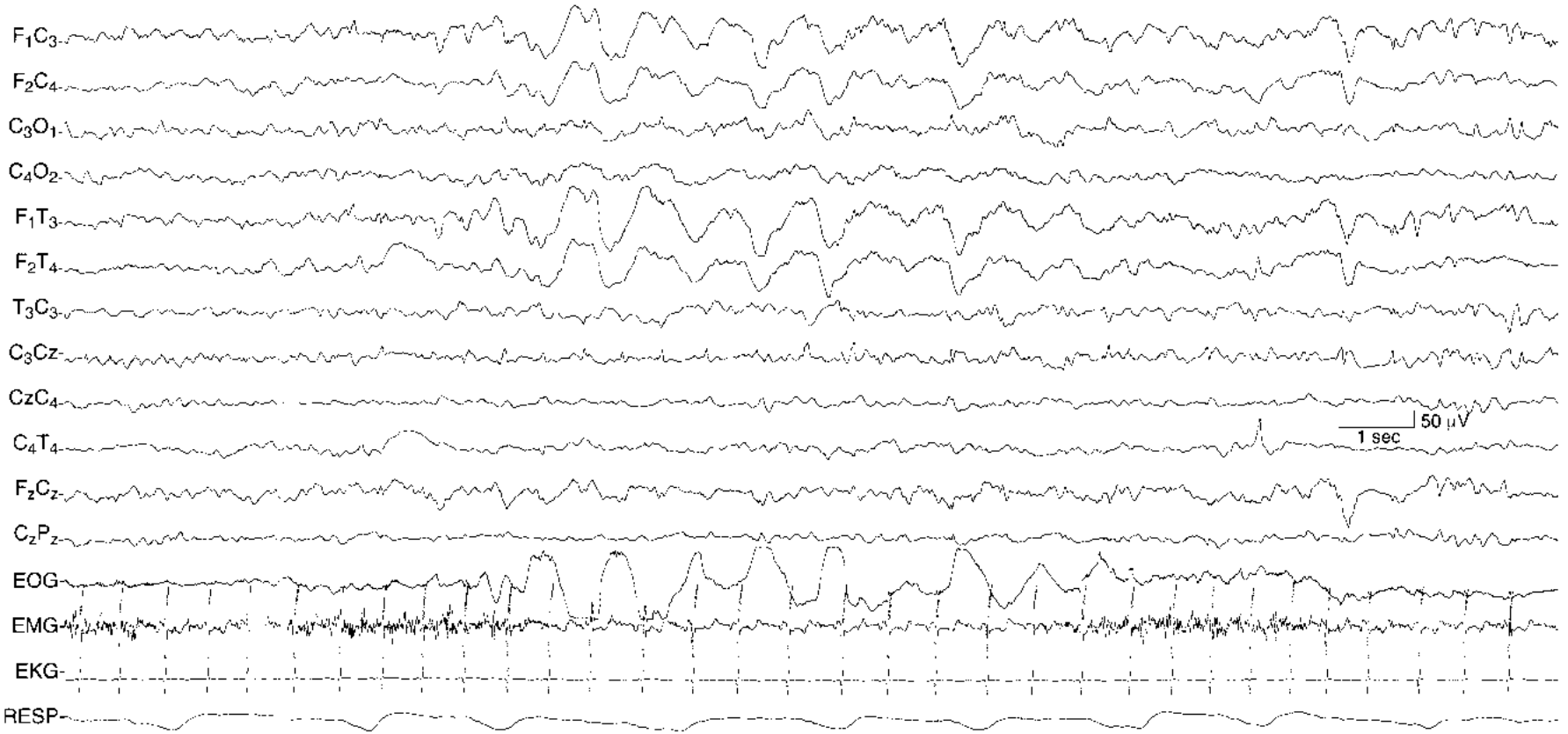

Figure 3.38 Slow activity associated with repetitive eye opening and closure. High voltage, slow activity is present in the frontal regions bilaterally associated with rhythmic eye opening and closure. This activity is also present in the EOG channel. The EEG background activity is within the range of normal variation in this 39-week CA infant.

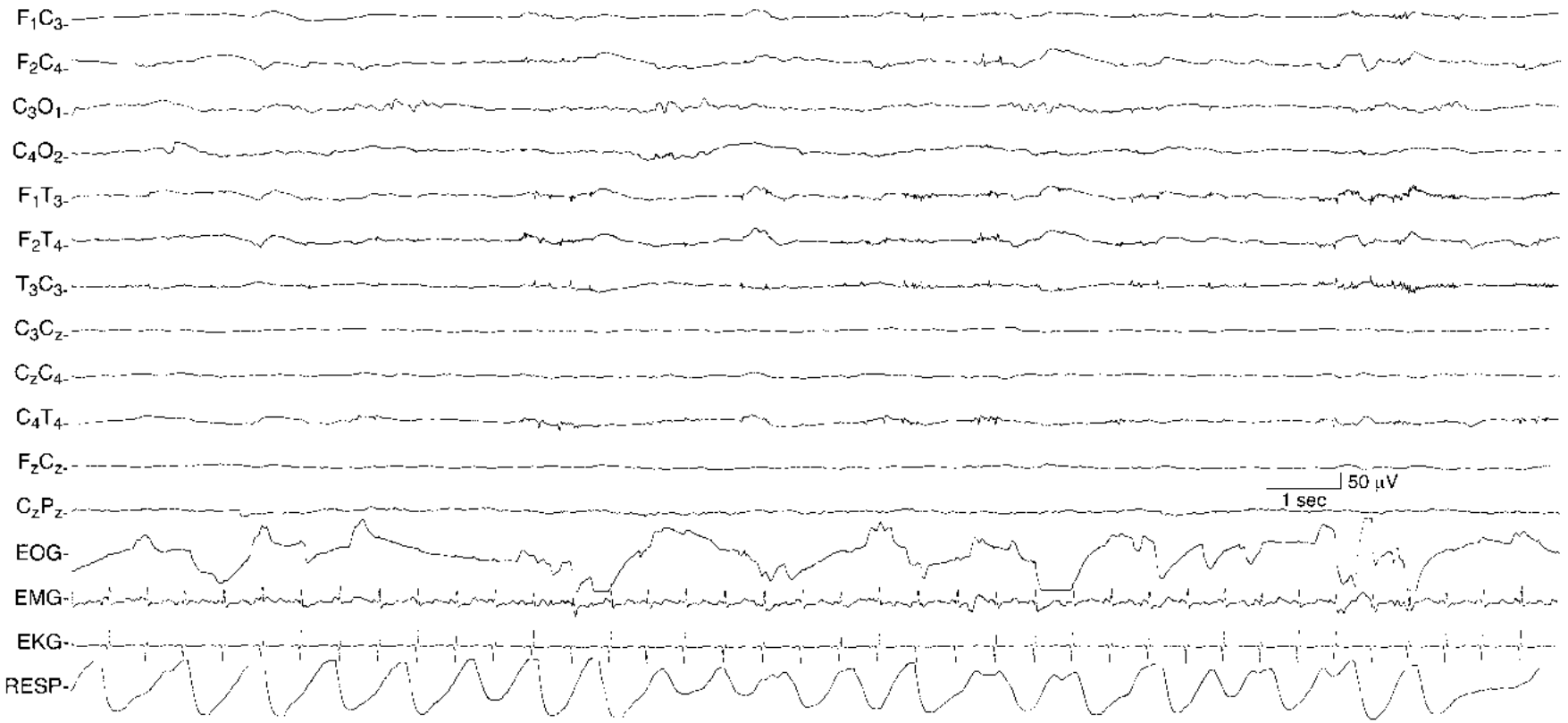

Figure 3.39 Random EMG potentials from facial muscles. Random low voltage EMG potentials are present in the left and right temporal regions and, rarely, in the right frontal region, associated with twitches of facial muscles. The background activity is depressed and undifferentiated in this 41-week CA infant.

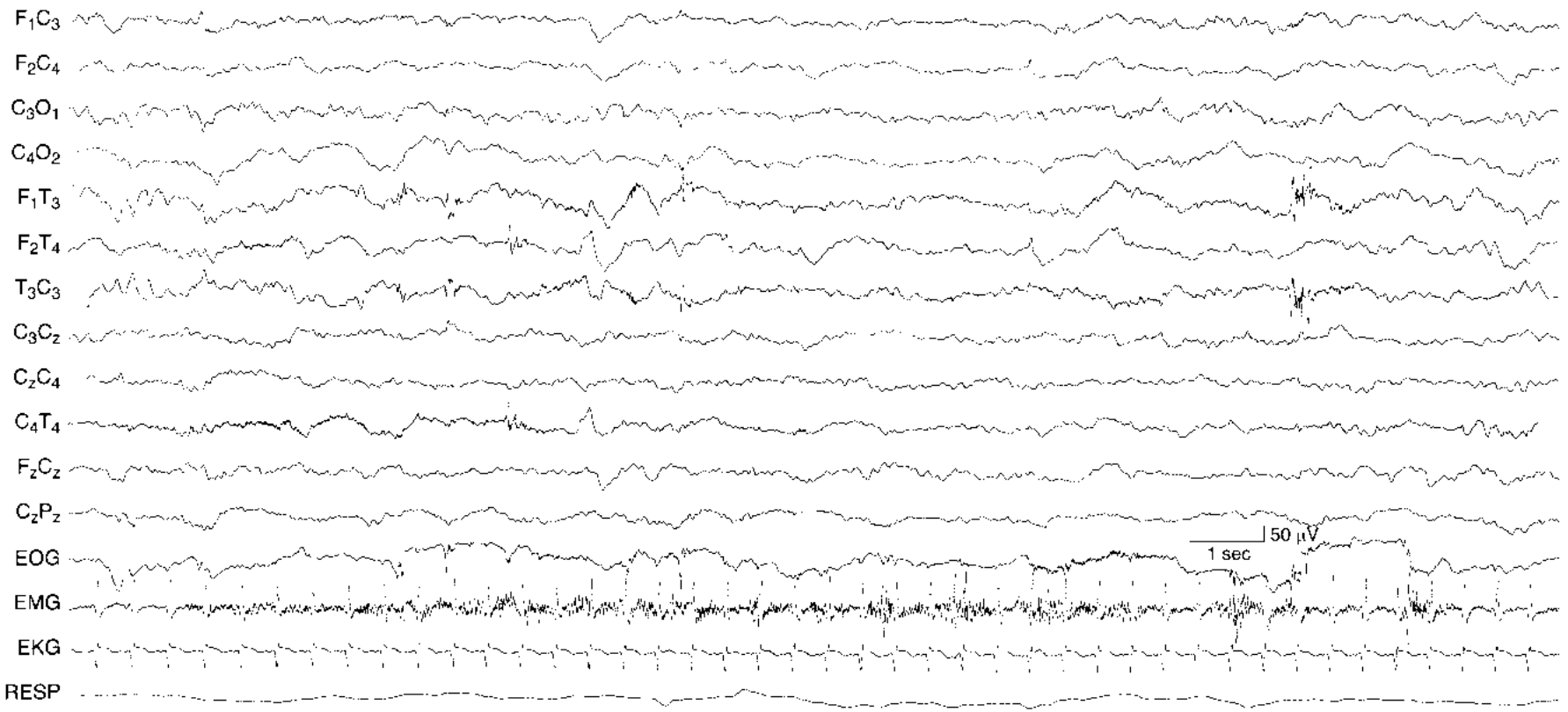

Figure 3.40 Multifocal and complex EMG potentials from facial muscles. Spike-like potentials are present in the left and right temporal regions and a more complex burst of EMG activity is present later in the left temporal region in this 39-week CA infant with normal EEG background activity.

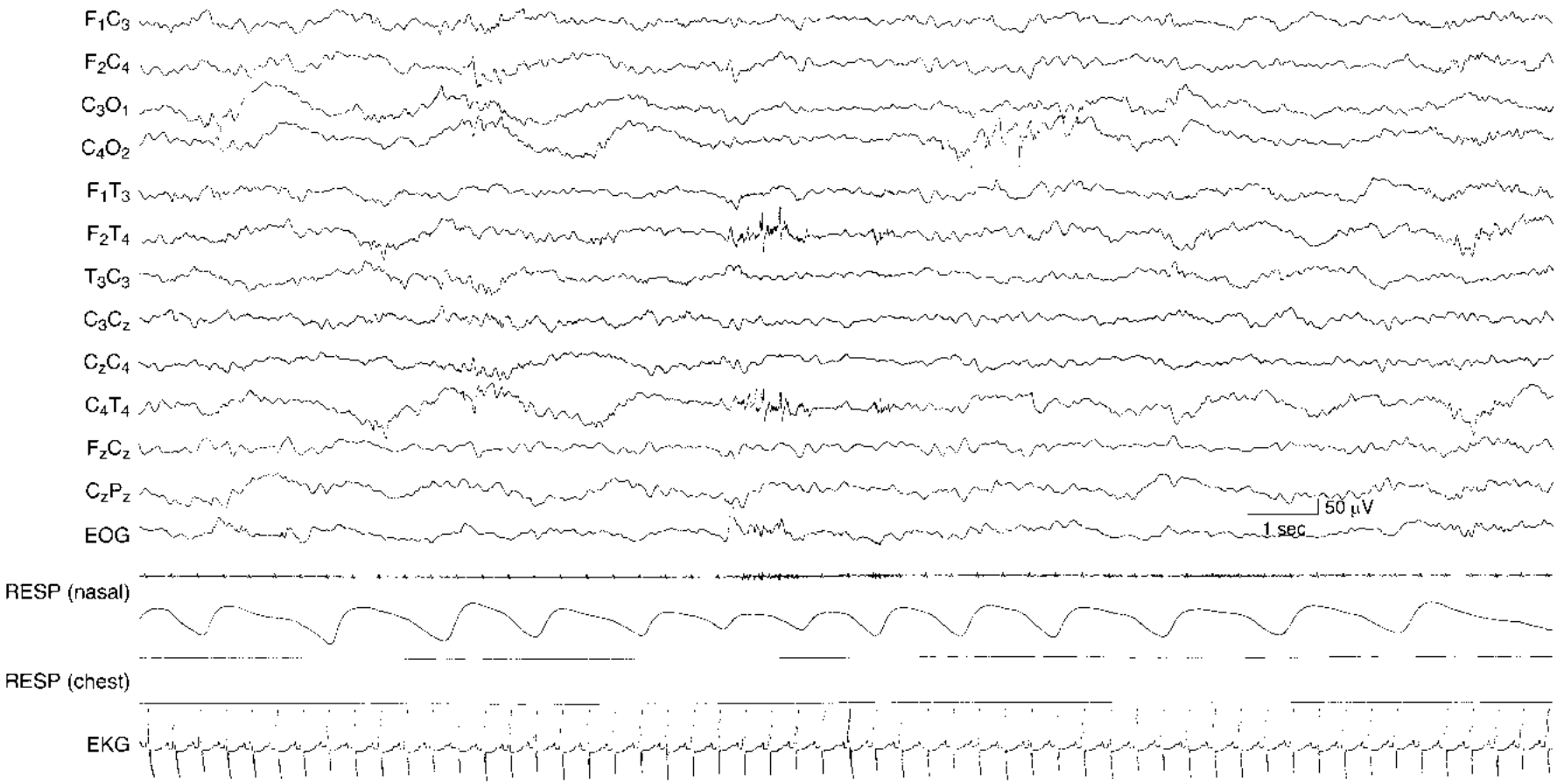

Figure 3.41 Brief rhythmic EMG potentials from facial muscles compared with occipital sharp waves. A burst of EMG activity is present in the right temporal region in the early portion of this sample. During the latter portion of the recording a burst of spike and sharp wave activity of cerebral origin is present in the right occipital region (see Chapter 5) in this 39-week CA infant with otherwise normal EEG background activity.

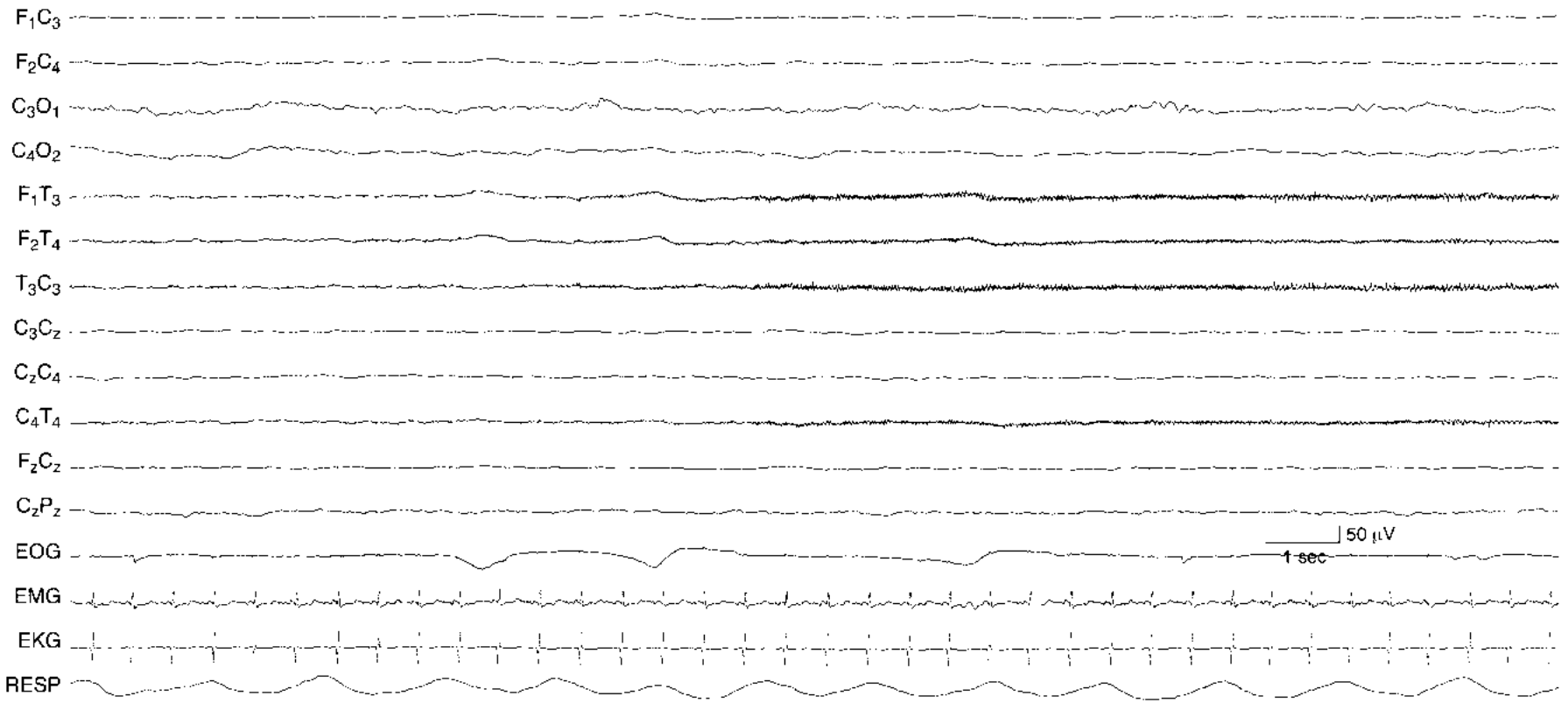

Figure 3.42 Build-up of sustained EMG in the temporal region. There is a build-up of sustained EMG activity in the temporal regions bilaterally, higher in amplitude on the left. The background EEG is depressed and undifferentiated in this 41-week CA infant.

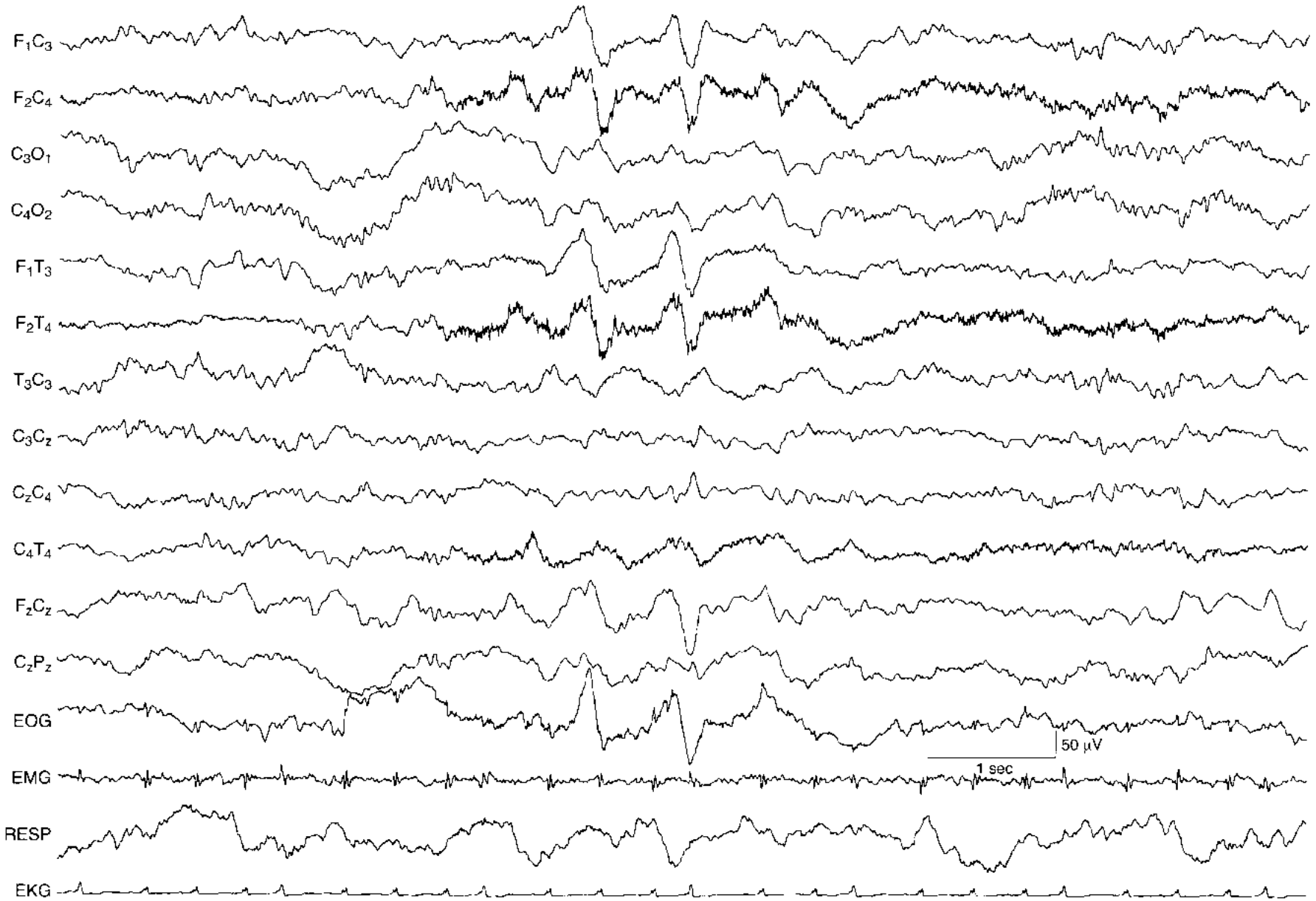

Figure 3.43 Build-up of sustained EMG in the frontal region. There is a brief build-up of EMG activity primarily in the right frontal region in this 37-week CA infant with normal EEG background activity.

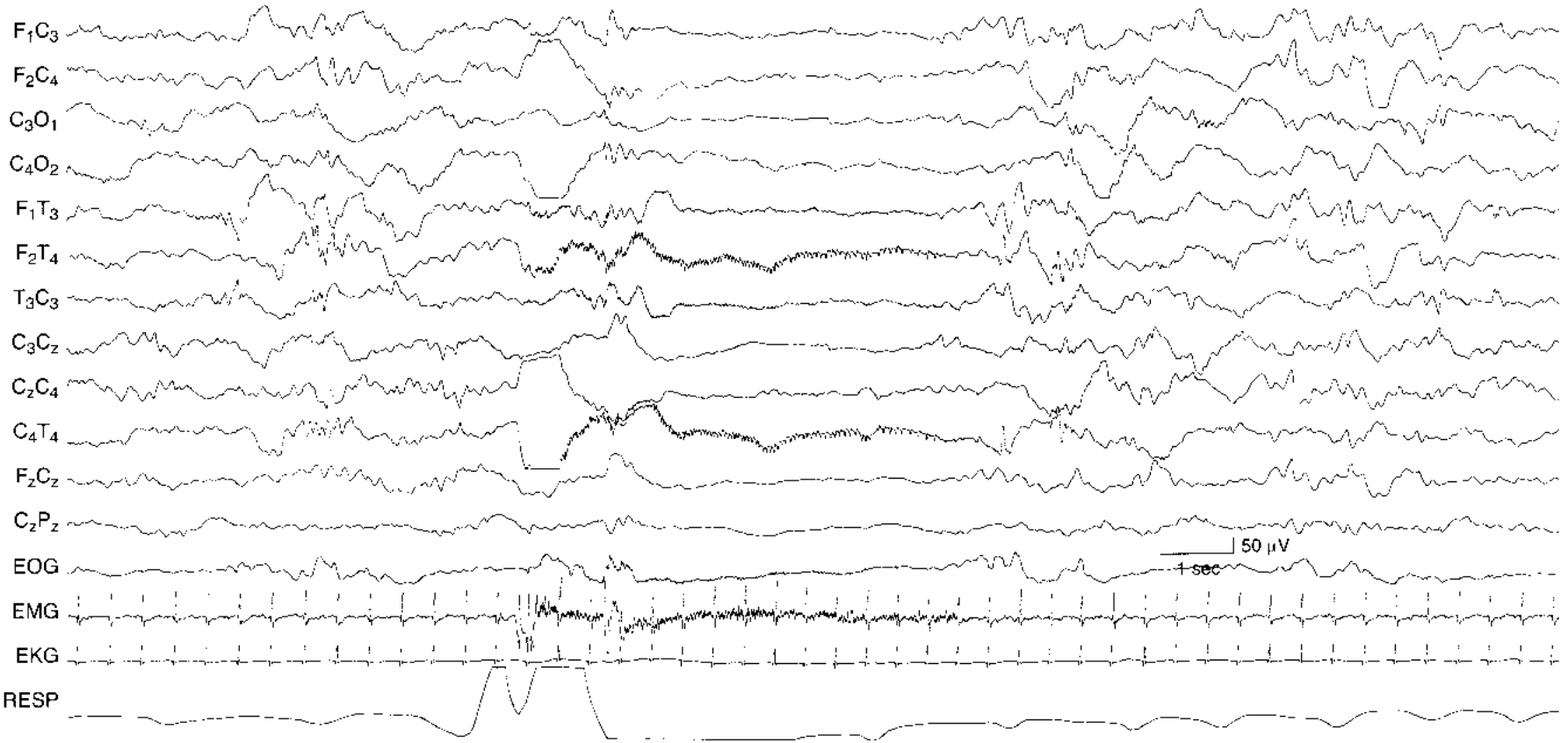

Figure 3.44 Build-up of sustained EMG in the temporal region associated with arousal. There is a burst of EMG activity in the right temporal region which eventually has a relatively slow rate of firing. This activity occurs with the spontaneous arousal of the infant that is associated on EEG with generalized voltage attenuation (see Chapter 4). The infant is 40-weeks CA with normal EEG background activity but with multifocal sharp waves of cerebral origin (see Chapter 5).

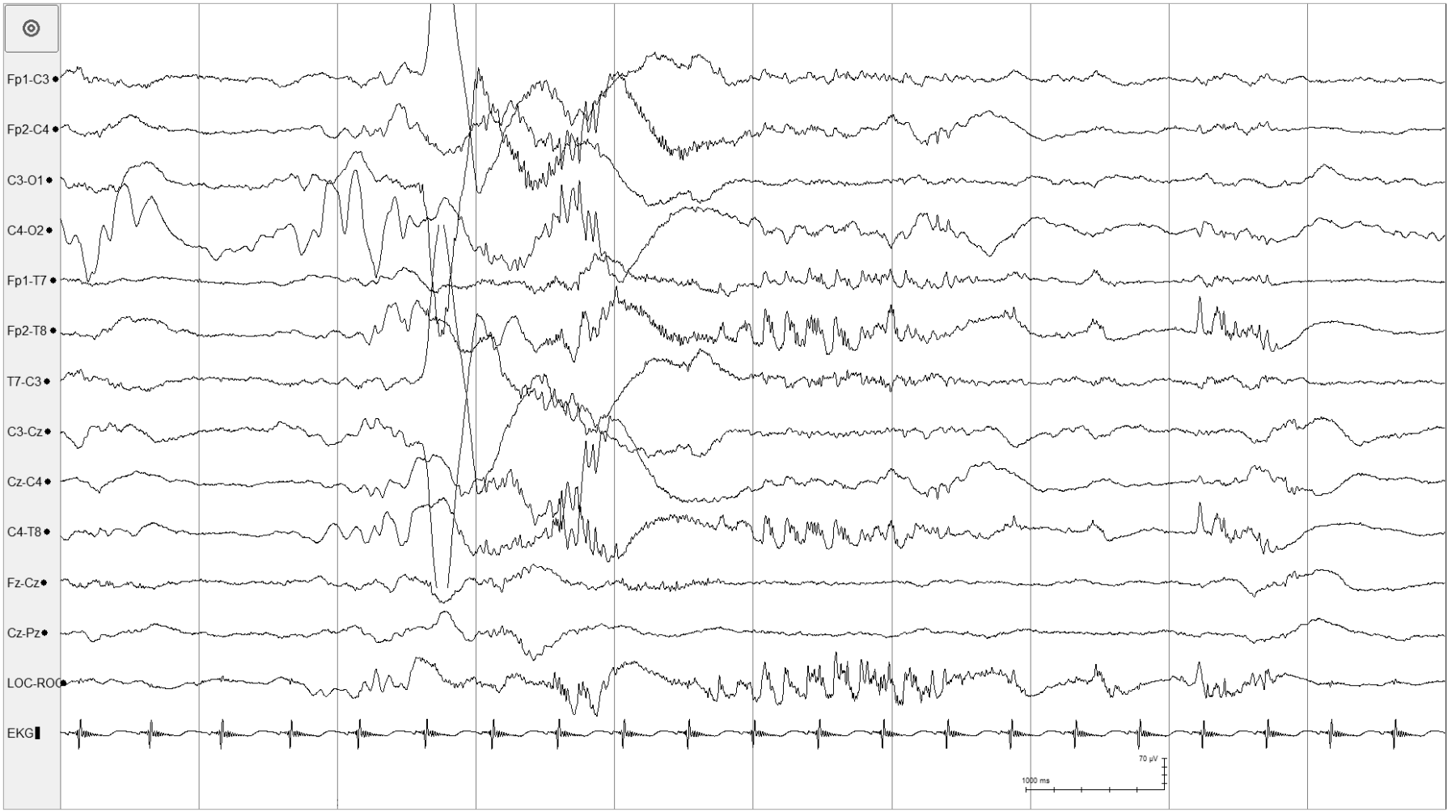

Figure 3.45 Rhythmic polymorphic sharp waves due to lip smacking. Rhythmic, irregularly shaped waves present in the right temporal region and EOG are associated with lip smacking activity in this 25-week CA infant with a normal *tracé discontinu* pattern.

Figure 3.46 Periodic EMG associated with fragmentary myoclonus. Periodic EMG potentials are present bilaterally, but most prominently on the right, associated with fragmented myoclonus in this 26-week CA infant during a period of a prolonged interburst interval on EEG.

CHAPTER 4

Elements of the Normal Neonatal EEG

Visual analysis of the neonatal electroencephalogram (EEG) requires the recognition of the conceptional age-dependent features characteristic of specific epochs of development. These electrographic features are presented here in four different formats: a table that lists specific elements (**Table 4.1**), a narrative that describes the continuum of development, and a summary by epoch of conceptional age (CA) of the expected elements. In addition, representative samples of EEG recordings in each epoch are provided.

Visual analysis and interpretation require determination of the degree of continuity of background activity (**Figure 4.1**), and a degree of interhemispheric synchrony of the background activity (**Figure 4.2**). They also require recognition of specific waveforms and patterns that occur with increasing age (**Figure 4.3**), the appearance of wake/sleep cycles (Dos Santos et al., 2014; Dreyfus-Brisac, 1968; Scher, 2011), and the age-dependent response of the EEG to stimulation of the infant.

CONTINUUM OF DEVELOPMENT

Continuity

When the brain's electrical activity, as revealed by the EEG first appears, it is discontinuous, with long periods of quiescence; this pattern is referred to as *tracé discontinu* (Dreyfus-Brisac, 1962). As age increases, periods of inactivity shorten (**Figure 4.1**) (Anderson et al., 1985; Connell et al., 1978; Hahn et al., 1989; Selton et al., 2000). The longest acceptable single interburst-interval durations in relation to CA have been reported to be: 24 to 26 weeks CA, 60 seconds (Vecchierini et al., 2003); 26 weeks CA, 46 seconds; 27 weeks CA, 36 seconds; 28 weeks CA, 27 seconds (Selton et al., 2000); less than 30 weeks CA, 35 seconds; 31 to 33 weeks CA, 20 seconds; 34 to 36 weeks CA, 10 seconds; and 37 to 40 weeks CA, 6 seconds (Clancy et al., 2003; Hahn et al., 1989).

At a CA of approximately 30 weeks, continuous activity appears and is present only during rapid eye movement (REM) sleep. At about 34 weeks CA, the EEG is also continuous in the awake state. This continuous polyfrequency pattern has been traditionally referred to as *activité moyenne* (Lamblin et al., 1999). Continuity appears in non-REM (NREM) sleep at about 36 to 37 weeks. However, from that time until about 5 to 6 weeks post-term, the EEG during periods of NREM sleep shows occasional semiperiodic episodes of generalized voltage, attenuation (not quiescence) lasting from 3 to 15 seconds; a pattern that has been called *tracé alternant* (Dreyfus-Brisac and Blanc, 1956). Examples of CA-dependent discontinuity are shown in **Figures 4.4 to 4.39.**

Bilateral Synchrony

Before 27 to 28 weeks CA, EEG activity typically occurs in generalized bisynchronous bursts with a discontinuous background in the interburst intervals (Selton et al., 2000). However, the bursts may also appear asynchronously (**Figure 4.8**). After 27 to 28 weeks CA, the activity is generally asynchronous in homologous regions of the hemispheres (the greater the distance from the midline, the greater the degree of asynchrony). With increasing maturity, the degree of asynchrony diminishes. The degree of asynchrony reflects not only maturation but also the wake/sleep state. Thus, asynchrony is most prominent in NREM sleep and is least prominent in REM sleep. The only exception to these general rules is that from the time frontal sharp waves first appear, at about 35 weeks CA, they are bilaterally synchronous. Examples of EEG demonstrating increasing interhemispheric synchrony with increasing CA are shown in **Figures 4.6 to 4.39**.

Table 4.1 Developmental EEG Characteristics of Premature and Term Infants

	Continuity of background activity			Synchrony of background activity between homologous leads					
Conceptional age (wk)	Awake	Quiet sleep	Active sleep	Awake	Quiet sleep	Active sleep	EEG difference between wakefulness and sleep	Appearance and disappearance of specific waveforms and patterns	Reactivity to stimulus
27–28	–	D	D	–	++++	++++	No		NR
29–30	D	D	D	0	0	0	No	1. Temporal theta bursts (4–6 Hz) 2. Beta–delta complexes in central regions 3. Occipital, very slow activity	NR
31–33	D	D	C	+	+	++	No	1. Beta–delta complexes in occipitotemporal regions 2. Rhythmic 1.5-Hz activity in frontal leads in transitional sleep 3. Temporal alpha bursts replace 4- to 5-Hz bursts (33 wk)	NR
34–35	C	D	C	+++	+	+++	No	1. Frontal sharp-wave transients 2. Extremely high voltage beta activity during beta–delta complexes 3. Temporal alpha bursts disappear	R
36–37	C	D	C	++++	++	++++	Yes	1. Continuous bioccipital delta activity with superimposed 12- to 15-Hz activity during active sleep 2. Central beta–delta complexes disappear	R
38–40	C	C	C	++++	+++	++++	Yes	1. Occipital beta–delta complexes decrease and disappear by 39 wk 2. *Tracé alternant* pattern during NREM sleep	R

Increasing degrees of synchrony are represented as: 0, total asynchrony; +, minimal synchrony to ++++, total synchrony. C, continuous activity; D, discontinuous activity; NR, nonreactive; R, reactive; NREM, nonrapid eye movement.

Source: From Hrachovy RA, Mizrahi EM, Kellaway P. Electroencephalography of the newborn. In: Daly DD, Pedley PA, eds. Current Practice of Clinical Neurophysiology. 2nd ed. Philadelphia: Lippincott-Raven; 1991: 202, with permission.

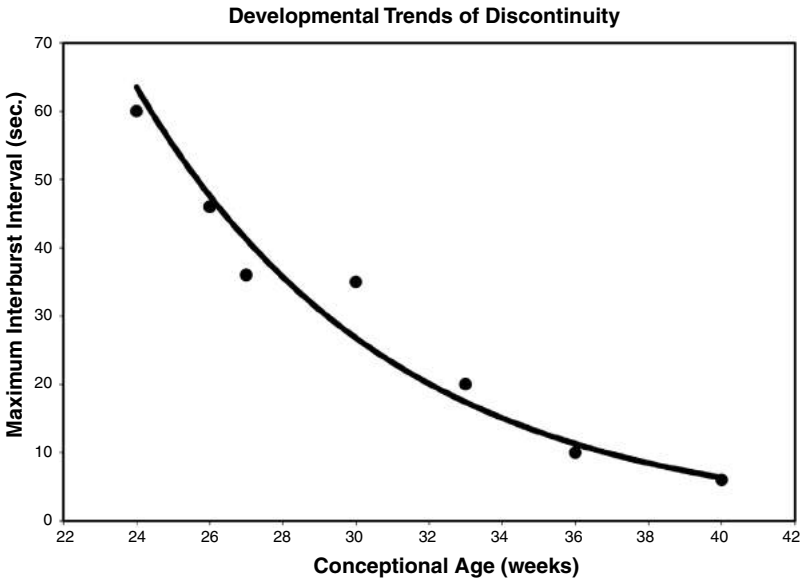

Figure 4.1 Average duration of discontinuous periods in NREM sleep in the EEG of a premature infant. Data points are taken from Verrichierni et al. (2003) (24–26 weeks CA), Selton et al. (2000) (26–28 weeks CA), and Hahn et al. (1987), Clancy et al. (2003) (30–40 weeks CA) and a curve derived from exponential regression.

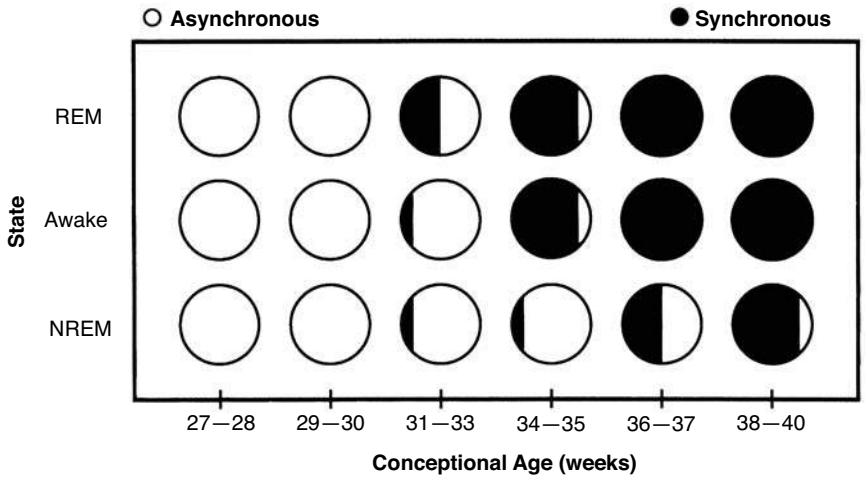

Figure 4.2 Development of interhemispheric synchrony in the EEG of the premature infant. See text for details and references. (Hrachovy, 2000, with permission.)

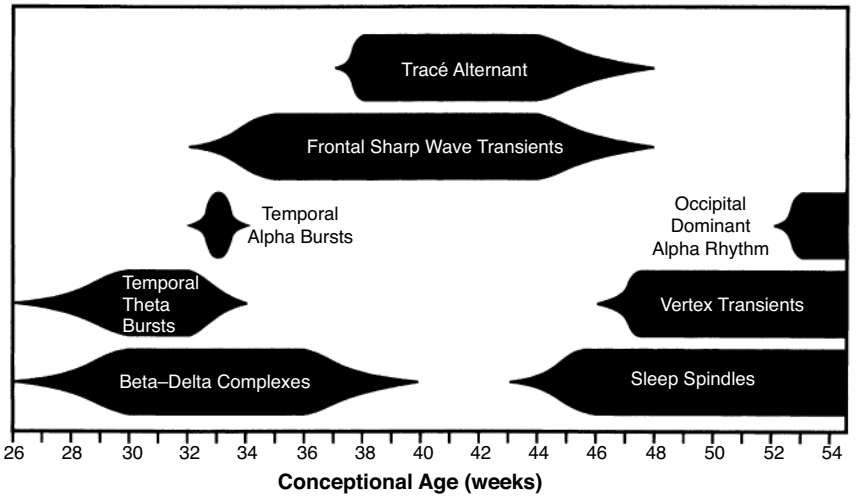

Figure 4.3 Appearance and disappearance of developmental EEG landmarks from prematurity to 3 months post-term. See text for details and references. (Hrachovy, 2000, with permission.)

EEG Developmental Landmarks

An orderly appearance and disappearance of specific waveforms and patterns occurs with increasing CA **(Figure 4.3)**.

Beta–Delta Complexes

The presence of these complexes constitutes the prime hallmark of prematurity and is present from about 26 to 38 weeks CA. They consist of random 0.3- to 1.5-Hz waves of 50 to 250 μV, with superimposed bursts of low- to moderate-voltage fast activity. The frequency of the fast activity may vary, even in the same infant. Two frequencies predominate: 8 to 12 Hz and, more commonly, 18 to 22 Hz. The voltage of the fast activity varies throughout each burst but rarely exceeds 75 μV. **Figures 4.6 to 4.22** show typical beta–delta complexes at varying CAs. Various names have been given to these complexes: "spindle-delta bursts," "brushes," "spindle-like fast waves," and "ripples of prematurity." Dreyfus-Brisac et al. (1956), who first described the complexes, referred to them as "rapid bursts," emphasizing, as in other names, the fast component. An important feature of beta–delta complexes is that they typically occur asynchronously in derivations from homologous areas and show a variable voltage asymmetry on the two sides.

These complexes first appear as a dominant feature in the EEG at about 26 weeks CA. When first present, these occur infrequently and largely in the

central regions. During the next 5 to 6 weeks, they become progressively more persistent, and the voltage of the fast component usually increases. Until 32 weeks CA, the fast component has a predominant frequency of 18 to 22 Hz; thereafter, the slower frequency (8–12 Hz) is most often present. The special distribution of the beta–delta complexes also changes with CA, becoming more prominent in the occipital and temporal regions with increasing age.

From the time beta–delta complexes first appear and changes in the wake/sleep cycle can be appreciated, the presence of beta–delta complexes is a prominent feature during REM sleep—a state characterized by virtually continuous EEG activity after 30 weeks CA. At 33 weeks CA, beta–delta complexes are maximally expressed in NREM sleep, rather than REM sleep, and appear more prominently in the temporal-occipital areas. From 33 to 37 weeks CA, beta–delta complexes continue to occur primarily in NREM sleep.

Temporal Theta and Alpha Bursts

A useful developmental EEG marker is the appearance of rhythmic 4 to 6 Hz waves occurring independently in short bursts of rarely more than 2 seconds arising independently in the left and right midtemporal areas. Voltage varies from roughly 20 to 200 μV. Individual waves often have a sharp configuration (Hughes et al., 1987; Werner et al., 1977) (**Figures 4.10**, **4.11**, **4.13**–**4.15**). This activity appears at about 26 weeks CA, is expressed maximally between 30 and 32 weeks, and then rapidly disappears. It is replaced by temporal alpha bursts that otherwise have characteristics of amplitude, burst duration, and spatial distribution similar to temporal theta bursts (**Figures 4.16**–**4.18**). The presence of temporal alpha bursts can be considered a very specific marker for 33 weeks; they appear at that CA and are no longer present at 34 weeks CA.

Frontal Sharp Waves

Isolated sharp waves of blunt configuration, usually with an initial surface-negative phase followed by a surface-positive phase, have been referred to as *encouche frontales* (Dreyfus-Brisac, 1962; Kellaway and Crawley, 1964). They may be present at 34 weeks CA but attain maximum expression at about 35 weeks CA. They diminish in number and voltage after 44 weeks CA and are only rarely seen in infants older than 6 weeks post-term.

These frontal sharp transients are bilaterally synchronous and symmetrical from the time of their first appearance, although there may be some variable lateralization (**Figures 4.19** and **4.27**) (Crippa et al., 2007). The initial surface-negative component lasts about 200 msec. The succeeding surface-positive component lasts somewhat longer, but this is quite variable and is often difficult to measure because intervening background activity obscures the termination of the waveform (**Figures 4.20** and **4.24**–**4.28**). They typically occur randomly as single events, predominantly in transitional rather than in REM or NREM sleep. However, they may also recur in brief runs and may also be mixed with other normal features of near-term infants such as bifrontal delta activity (**Figures 4.26** and **4.28**–**4.29**).

Distinguishing Between the Waking and Sleep EEG

Until 36 to 37 weeks CA, distinguishing the various states of the wake/sleep cycle is based upon empirical factors such as behavior and polygraphic parameters. Eye opening is associated with the awake state, and eye closure is associated with sleep. Regular respiration, random eye movements, and variable muscle tone are associated with NREM sleep while irregular respiration, REMs and decreased muscle tone are associated with REM sleep.

Electrographically at about 30 weeks CA, the background activity is continuous in REM sleep and discontinuous during wakefulness and NREM sleep. However, the EEG activity in all states is characterized by the presence of beta–delta complexes with their CA-dependent abundance, spatial distribution, and degree of synchrony (**Figures 4.21**–**4.23**).

By 36 to 37 weeks CA, a clear distinction can be made between the waking EEG and the sleep EEG based upon their inherent features, without reliance on clinical or polygraphic data (**Figures 4.31**–**4.37**). In the awake EEG, beta–delta complexes are rarely present and the awake background activity consists chiefly of continuous polyfrequency activity, traditionally referred to as *activité moyenne*. This polyfrequency activity is characterized by random, very slow, low-voltage activity best described as baseline shifting, with superimposed semirhythmic 4 to 8 Hz activity in all regions. In addition generalized, very low voltage 18 to 22 Hz activity and anteriorly distributed, very low voltage 2 to 3 Hz activity may be present. From the standpoint of determining CA, disappearance of the beta–delta complexes when the infant appears behaviorally awake constitutes an important marker of 36 to 37 weeks CA.

Before about 36 weeks CA, the background activity in NREM sleep is discontinuous (**Figure 4.22**). Between 36 and 38 weeks CA, two NREM EEG patterns emerge. The first is continuous high-voltage slow-wave activity in all regions. The second pattern is known as *tracé alternant* and is characterized by a modulation of generalized activity with alternating periods of high and low voltage activity (**Figures 4.33**–**4.35**). This pattern may occur in infants through 44 weeks CA. After that period, NREM sleep is characterized by continuous slow-wave activity with the eventual emergence of sleep spindles after about 46 weeks CA—although rudimentary spindles may occur earlier (**Figures 4.38** and **4.39**).

The EEG character of REM sleep is similar to that of the awake recording from about 30 weeks CA. Infant behaviors and polygraphic recordings

of respiration, eye movements, and submental EMG distinguish awake from REM sleep.

The terms *transitional sleep* or *indeterminant sleep* are used to characterize the state of the infant when it cannot be precisely determined by specific EEG criteria.

Reactivity to Stimulation

Changes in EEG activity in response to stimuli do not clearly emerge until about 33 to 34 weeks CA (**Figure 4.23**), and by 37 weeks CA, these responses can be easily elicited. The response to a stimulus is related to the character of the ongoing activity at the time of the stimulus. If high voltage, very slow activity is present, an effective stimulus may produce abrupt and pronounced generalized attenuation of voltage lasting as long as 5 to 10 seconds (Ellingson, 1958; Kellaway and Crawley, 1964).

Spontaneous episodes of attenuation may be associated with self-arousal (**Figures 4.23** and **4.37**). They occur in infants until about 2 months post-term, possibly in response to interoceptive stimuli. Such episodes should not be interpreted as evidence of immaturity or be confused with the repetitive episodes of generalized or regional attenuation that occur in abnormal conditions of diffuse cerebral dysfunction, such as neonatal encephalopathy.

Additional Special Waveforms and Patterns

Some special waveforms and patterns, particularly in the near-term and term infant, are considered to be within the range of normal variation although they are not developmental milestones, per se. They are bifrontal delta activity and some forms of temporal sharp waves.

Bifrontal Delta Activity

Bifrontal delta activity appears in the near-term or term infant as intermittent semirhythmic 1.5 to 2 Hz high-voltage activity in the frontal regions bilaterally (**Figures 4.28** and **4.29**). This activity may occur in close association with frontal sharp transients, most prominently during transitional sleep. This pattern has been referred to as "anterior dysrhythmia." However, this is a misnomer, because its presence does not suggest abnormality and it is considered within the range of normal variation (Clancy et al., 2003).

Temporal Sharp Waves

Temporal sharp waves are discussed in detail in the following chapter that concerns findings of uncertain diagnostic significance. That discussion describes criteria used to differentiate normal temporal sharp waves from those that are clearly abnormal. Temporal sharp waves that can be considered to be normal have a simple diphasic morphology, with the initial component appearing as surface-negative polarity, and occur randomly, usually asynchronously on the two sides and during sleep (**Figure 4.30**). Complex morphology, positive polarity, persistent localization and occurrence during wakefulness, are criteria for abnormality (see Chapter 5).

SUMMARY OF CONCEPTIONAL AGE-DEPENDENT FINDINGS

24 to 26 Weeks Conceptional Age (Figures 4.4 and 4.5)

- **Continuity**. There are brief bursts of activity between periods of electrical quiescence. The interburst interval is CA dependent and is at its longest at this age.
- **Synchrony**. Bursts of activity during this epoch are typically synchronous, but may also appear asynchronously on the two sides.
- **Landmarks**. Beta–delta complexes may be present during this epoch.
- **Wake/sleep cycles**. Cycles are not well defined by behavior or polygraphic changes. No evidence is seen on EEG of wake/sleep cycling.
- **Reactivity**. No reactivity to stimulation occurs.

27 to 28 Weeks Conceptional Age (Figures 4.6–4.8)

- **Continuity**. Electrical activity is episodic. Brief periods of generalized moderate-voltage activity may appear between periods of generalized electrical quiescence. The interburst intervals are relatively long compared to those present at later ages.
- **Synchrony**. The bursts of electrical activity are asynchronous on the two sides.
- **Landmarks**. Beta–delta complexes are present in the central region and rudimentary temporal theta bursts are present.
- **Wake/sleep cycles**. Cycles are not well defined by behavior or polygraphic changes. No evidence of wake/sleep cycles is found on EEG.
- **Reactivity**. No reaction to stimulation occurs.

29 to 30 Weeks Conceptional Age (Figures 4.9–4.12)

- **Continuity**. The EEG remains discontinuous, although brief periods occur in which behavioral and physiologic parameters suggest REM sleep when the EEG activity is relatively continuous. When the EEG is discontinuous, the duration of the interburst intervals is CA dependent and is less than in preceding epochs.

- **Synchrony**. Asynchrony between the two hemispheres is a predominant feature.
- **Landmarks**. Beta–delta complexes are present in the central regions. Temporal theta bursts are a consistent feature during this epoch. Occipital slow (delta) activity emerges during this epoch.
- **Wake/sleep cycles**. The EEG is continuous during periods when behavioral and physiologic parameters indicate REM sleep. There is no clear-cut relation between the stages of wakefulness and sleep on EEG except for a tendency for greater continuity of the background activity during REM sleep.
- **Reactivity**. No reaction to stimulation occurs.

31 to 33 Weeks Conceptional Age (Figures 4.13–4.18)

- **Continuity**. Continuous activity remains an aspect of REM sleep, but the EEG is discontinuous at other times.
- **Synchrony**. The degree of synchrony between hemispheres increases; however, this epoch is still marked by asynchrony when compared to epochs of infants at older ages.
- **Landmarks**. Beta–delta complexes are present and are more prominent in the occipital and temporal regions than in the central regions. Temporal theta bursts persist until 32 weeks CA and are largely replaced by temporal alpha bursts at 33 weeks CA.
- **Wake/sleep cycles**. The EEG is continuous during REM sleep and discontinuous during wakefulness and NREM sleep.
- **Reactivity**. No reaction to stimulation occurs.

34 to 35 Weeks Conceptional Age (Figures 4.19–4.22)

- **Continuity**. During wakefulness and REM sleep the EEG is continuous, but is still discontinuous during NREM sleep, although the degree of discontinuity is less than during the previous epoch.
- **Synchrony**. Synchrony continues to be greater during this epoch than in early epochs, but asynchrony persists, chiefly in NREM sleep.
- **Landmarks**. Frontal sharp transients (*enchoches frontales*) become well-defined by week 35 CA, although they may appear in rudimentary form during week 34 CA. During this epoch, beta–delta complexes persist. Temporal alpha bursts disappear by 34 weeks CA.
- **Wake/sleep cycles**. The EEG is continuous during wakefulness and REM sleep, but discontinuous during NREM sleep.
- **Reactivity**. The background activity is reactive to stimulation of the infant. The response and its character are dependent upon the state of the infant at the time of stimulation (**Figures 4.23** and **4.37**).

36 to 37 Weeks Conceptional Age (Figures 4.23 and 4.24)

- **Continuity**. During wakefulness and REM sleep, the EEG is continuous, but episodes of discontinuity may occur in NREM sleep.
- **Synchrony**. Synchrony continues to be greater during this epoch than in earlier epochs, now with most of the activity synchronous on the two sides.
- **Landmarks**. Frontal sharp transients persist. During this epoch, beta–delta complexes become less frequent. No new characteristic waveforms emerge, although bifrontal delta activity (a normal phenomenon) may be present during this epoch.
- **Wake/sleep cycles**. EEG and physiologic features of wakefulness, REM sleep and NREM sleep are present. At 36 weeks CA, a clear distinction can be made, based upon EEG criteria, between the awake and NREM sleep.
- **Reactivity**. The background is reactive to stimulation.

38 to 40 Weeks Conceptional Age (Figures 4.25–4.37)

- **Continuity**. The EEG is continuous in all states of sleep and in wakefulness.
- **Synchrony**. All activity becomes synchronous on the two sides by 40 weeks CA.
- **Landmarks**. Frontal sharp transients persist. During this epoch beta–delta complexes disappear from NREM sleep and are not present after 40 weeks CA.
- **Wake/sleep cycles**. EEG and physiologic features of wakefulness, REM sleep and NREM sleep persist. During this epoch, during NREM sleep, a modulation of the amplitude of the slow activity occurs with alternating periods of high amplitude and low voltage (*tracé alternant*).
- **Reactivity**. The background is reactive to stimulation.

41 to 44 Weeks Conceptional Age (Figure 4.38)

- **Continuity**. The EEG is continuous in wakefulness and all stages of sleep.
- **Synchrony**. Synchrony is virtually complete as in the previous epoch.
- **Landmarks**. Frontal sharp transients persist. No other immature waveforms are present.
- **Wake/sleep cycles**. Wakefulness and all stages of sleep are present. *Tracé alternant* begins to resolve by 44 weeks CA. NREM sleep is characterized by continuous slow-wave activity. Toward the end of this epoch rudimentary sleep spindles may appear. By 46 to 48 weeks CA, they are seen in all infants (**Figure 4.39**).
- **Reactivity**. The background is reactive to stimulation.

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45 to 48 Weeks Conceptional Age

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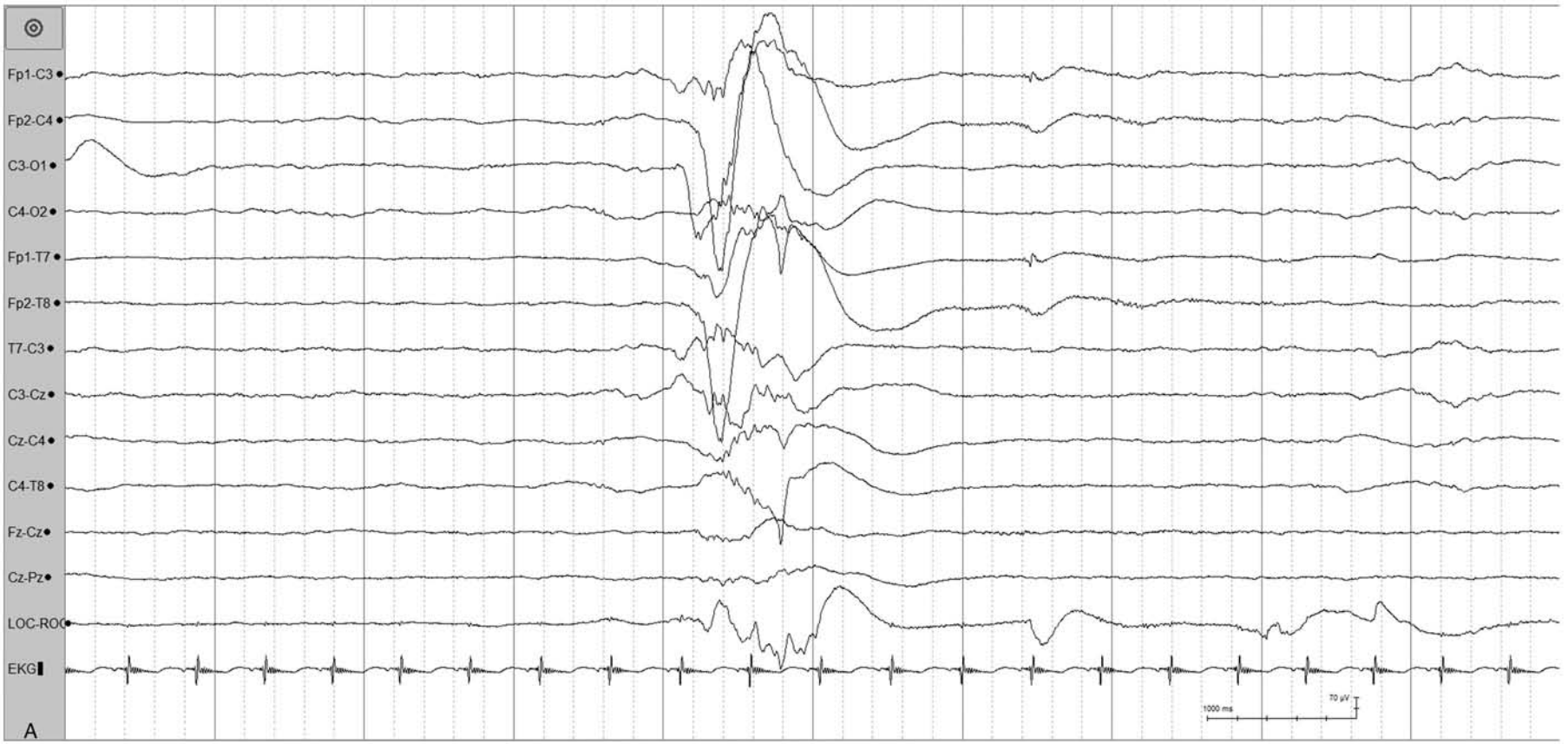

Figure 4.4 (A) and (B) 24 to 26 weeks CA. *Tracé discontinu* and bursts of bilaterally synchronous slow waves with superimposed fast activity. (A) This pattern is present in this 26-week CA infant. (*continued*)

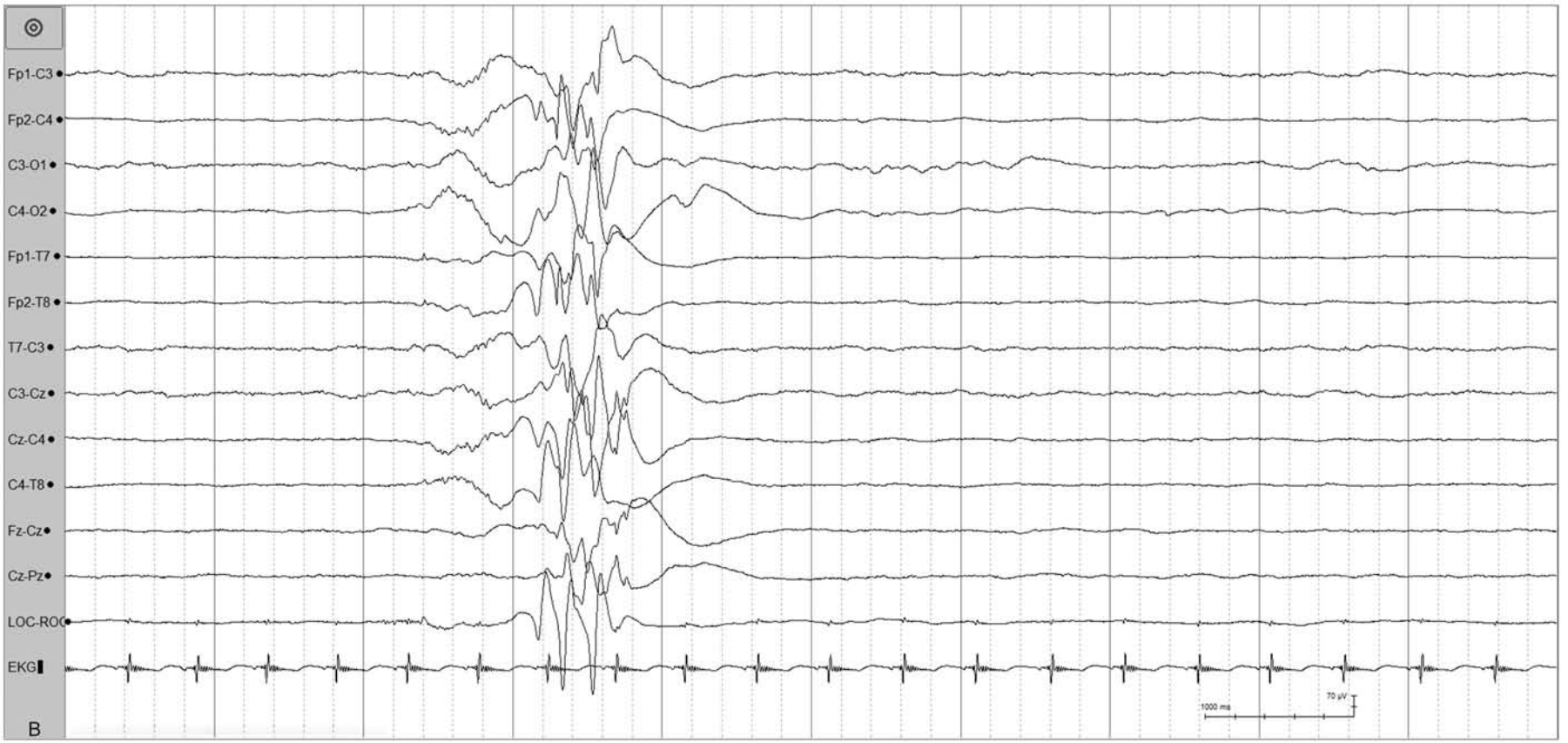

Figure 4.4 (*continued*) **(B)** Bilaterally synchronous burst with polyfrequency activity in the same infant.

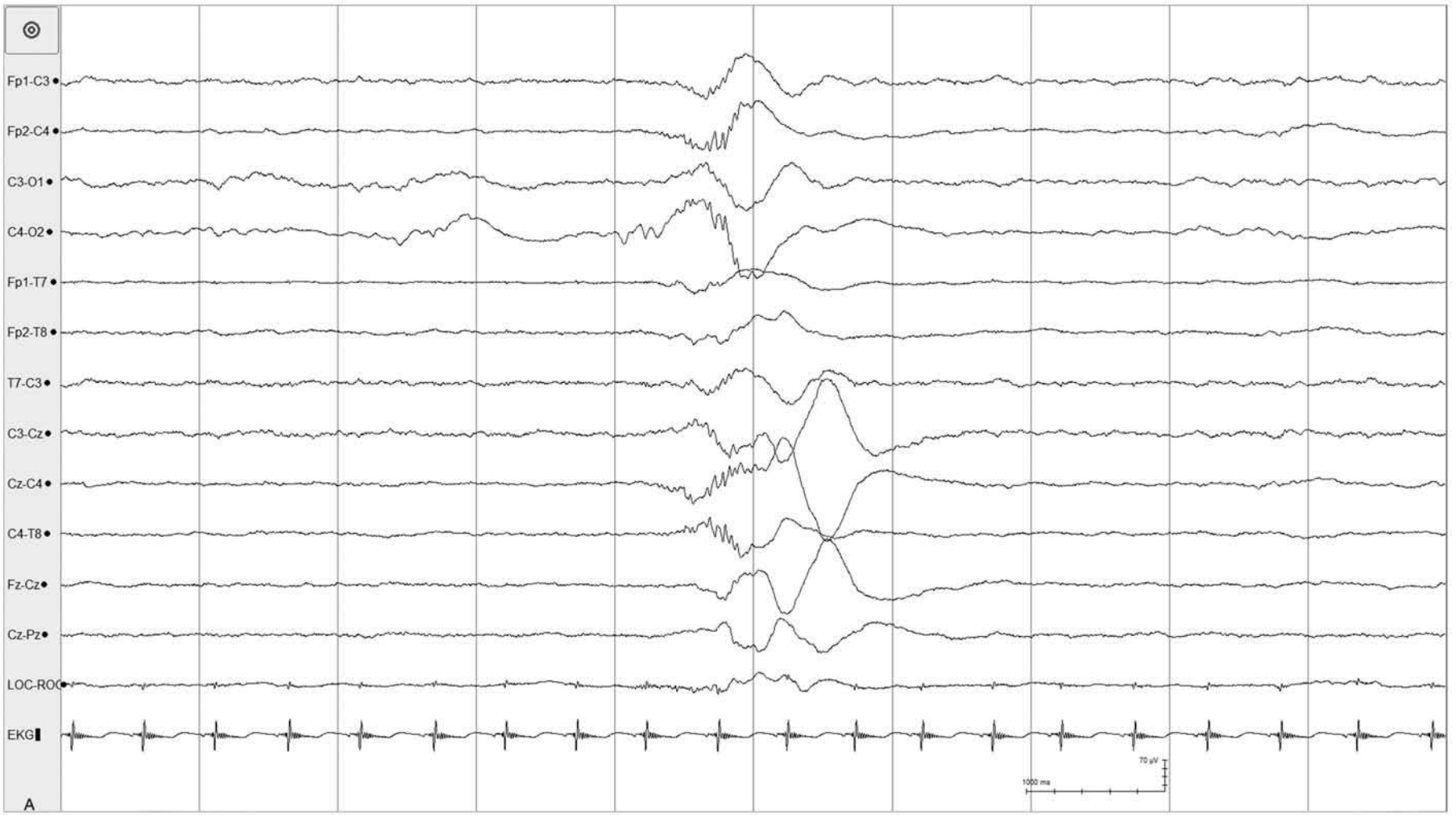

Figure 4.5 (A) and (B) 24 to 26 weeks CA. *Tracé discontinu* and bursts of bilaterally synchronous and asynchronous slow waves with superimposed fast activity. A burst of bilaterally synchronous beta–delta complexes in this 26-week CA infant. (*continued*)

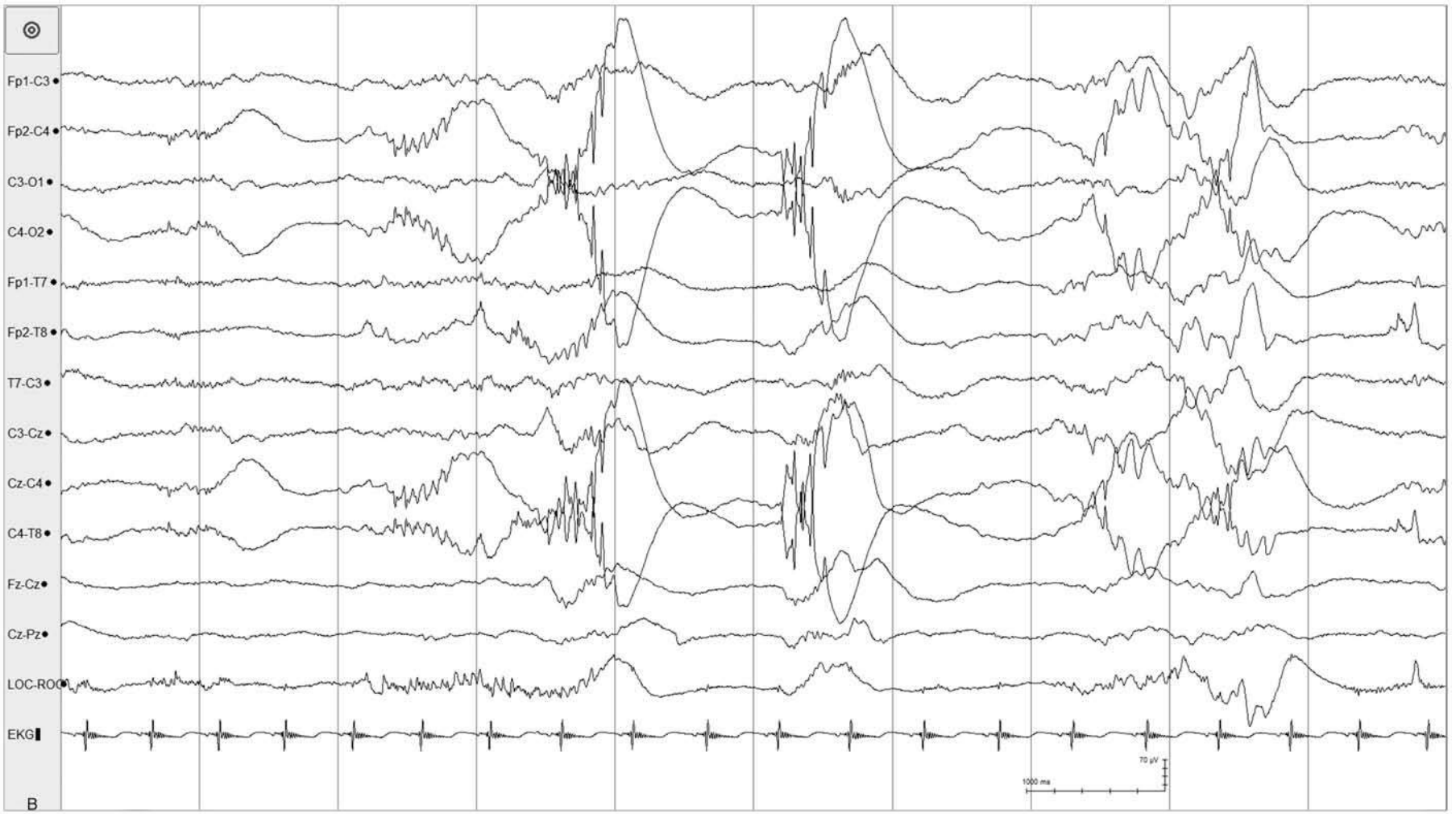

Figure 4.5 (*continued*) There are interburst intervals of varying durations in the same infant.

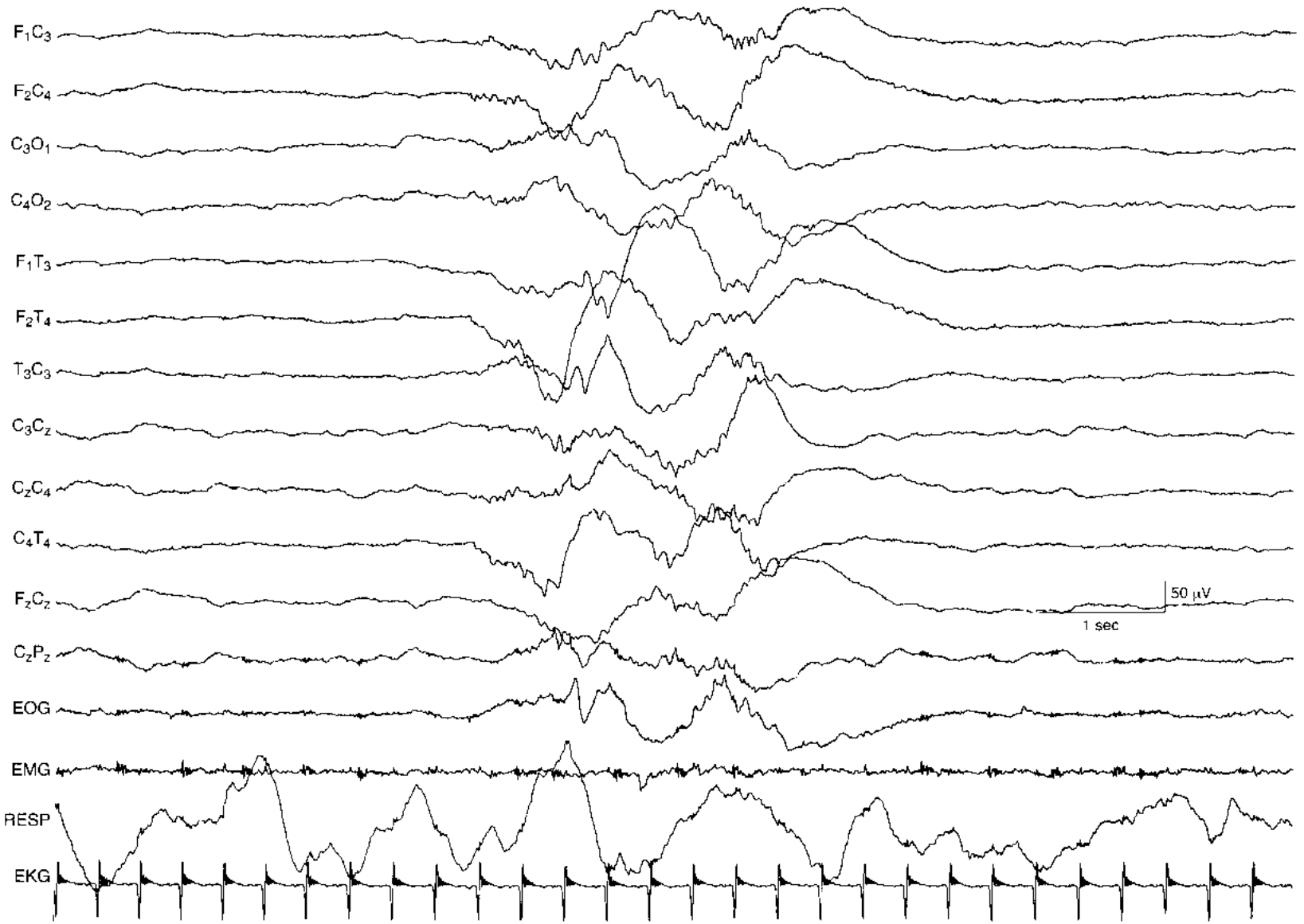

Figure 4.6 27 to 28 weeks CA. *Tracé discontinu* and a burst of bilateral, polyfrequency activity. The EEG demonstrates a *tracé discontinu* pattern. A burst of bilaterally symmetrical, somewhat asynchronous activity is present. This activity is slow with superimposed waves of faster frequency that resemble beta–delta complexes.

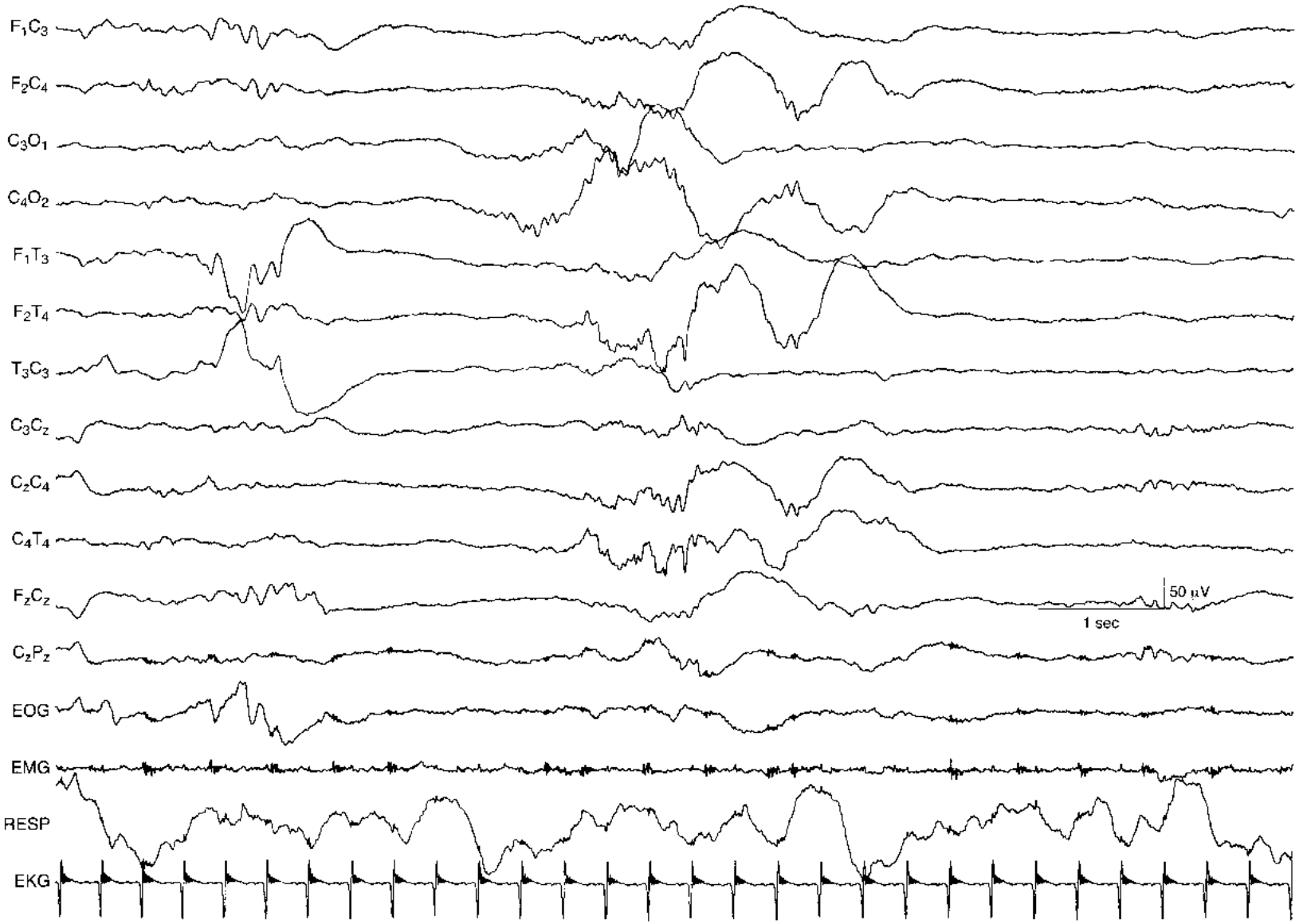

Figure 4.7 27 to 28 weeks CA. Central beta–delta complexes and temporal theta burst. The background is characterized by *tracé discontinu*. Beta–delta complexes are present, predominately in the right central region. A rudimentary theta burst is present in the left temporal region.

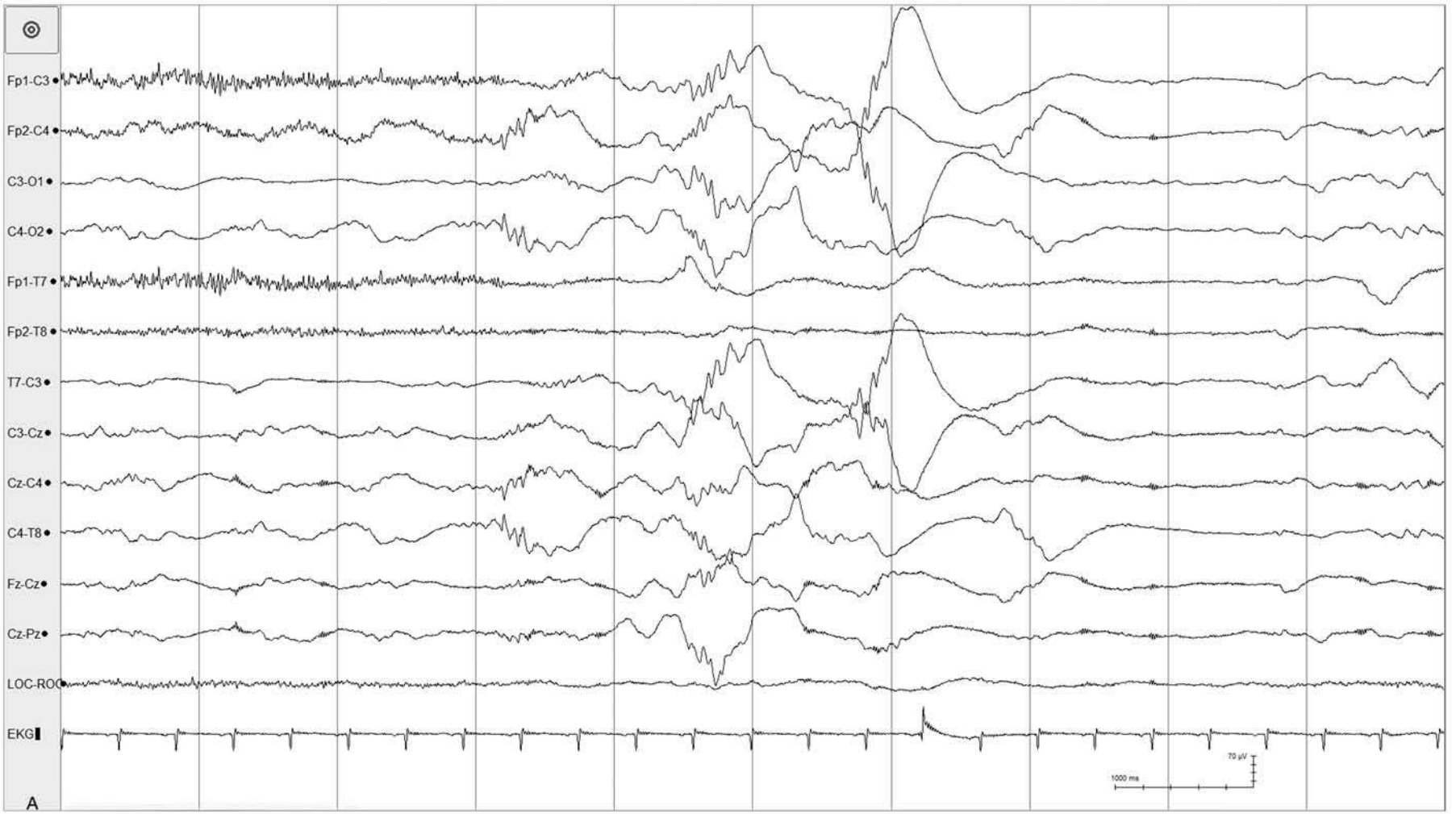

Figure 4.8 27 to 28 weeks CA. (A)–(C) *Tracé discontinu* and with asynchronous bursts of beta–delta complexes.
(A) Bursts appear predominantly in the left and right central regions. (*continued*)

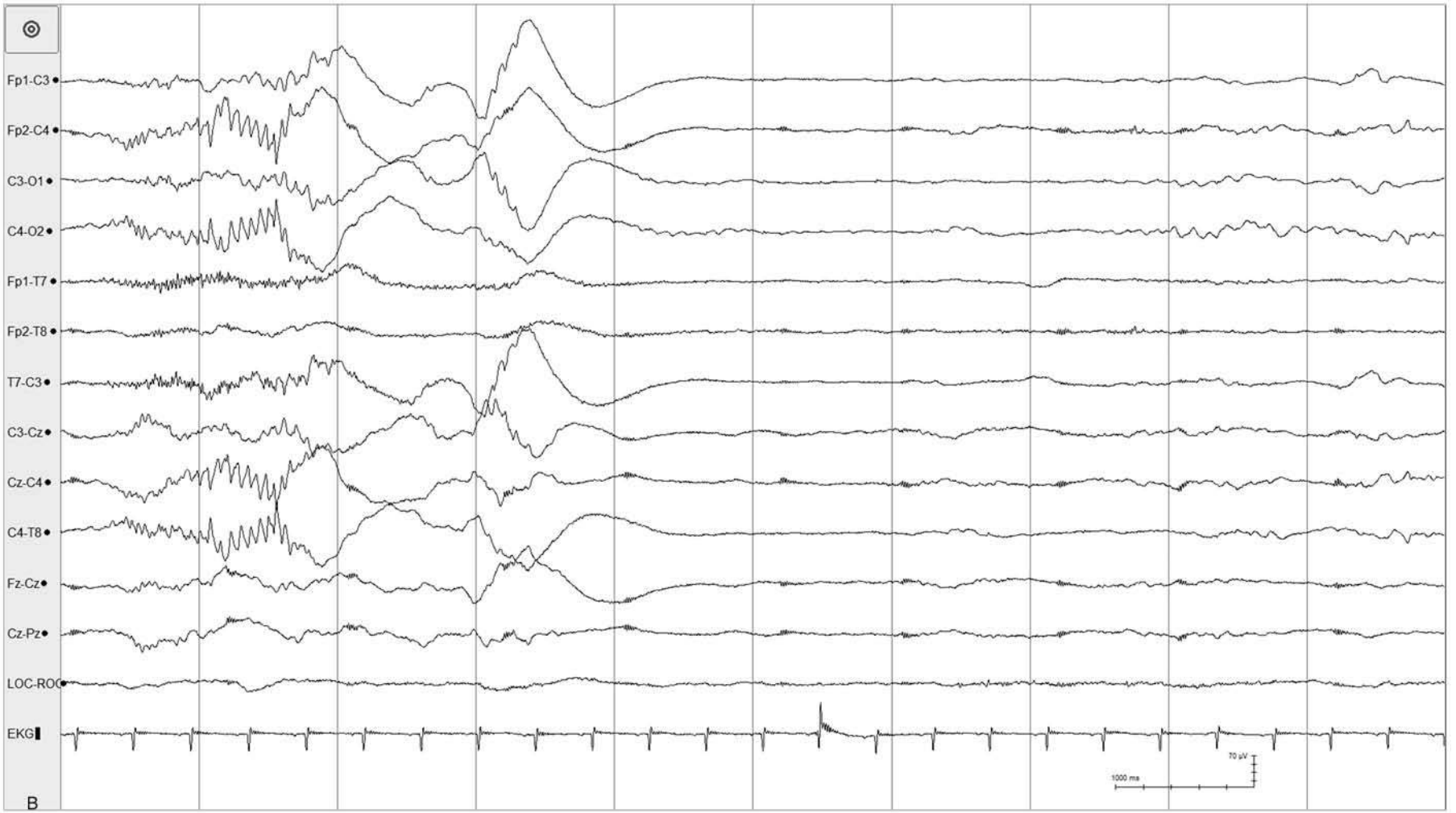

Figure 4.8 (*continued*) **(B)** Bursts appear predominantly in the right central region and also present in the left central region. (*continued*)

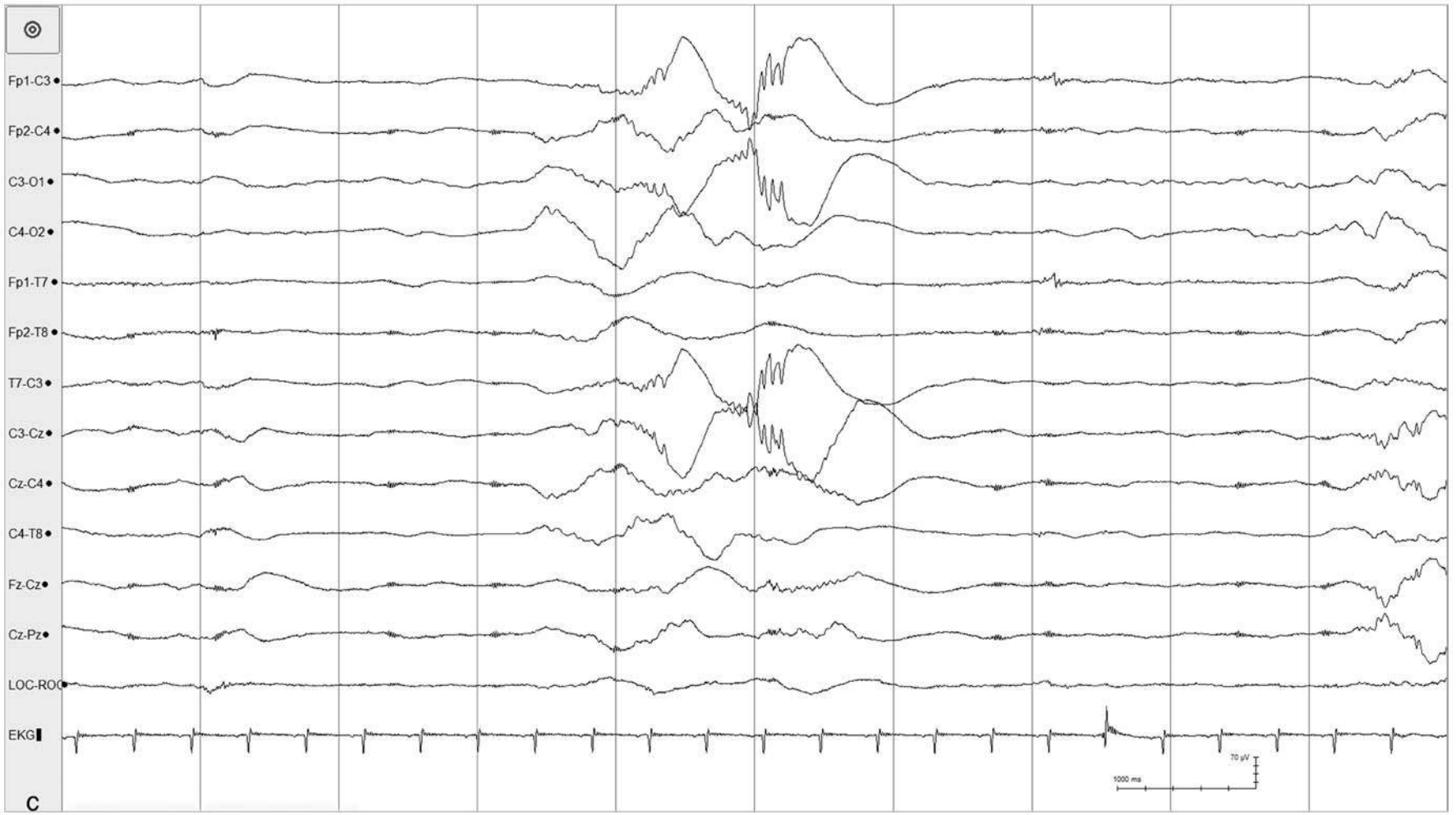

Figure 4.8 (*continued*) **(C)** Bursts appear in the left central region. All samples from the same recording of a 26- to 28-week CA infant.

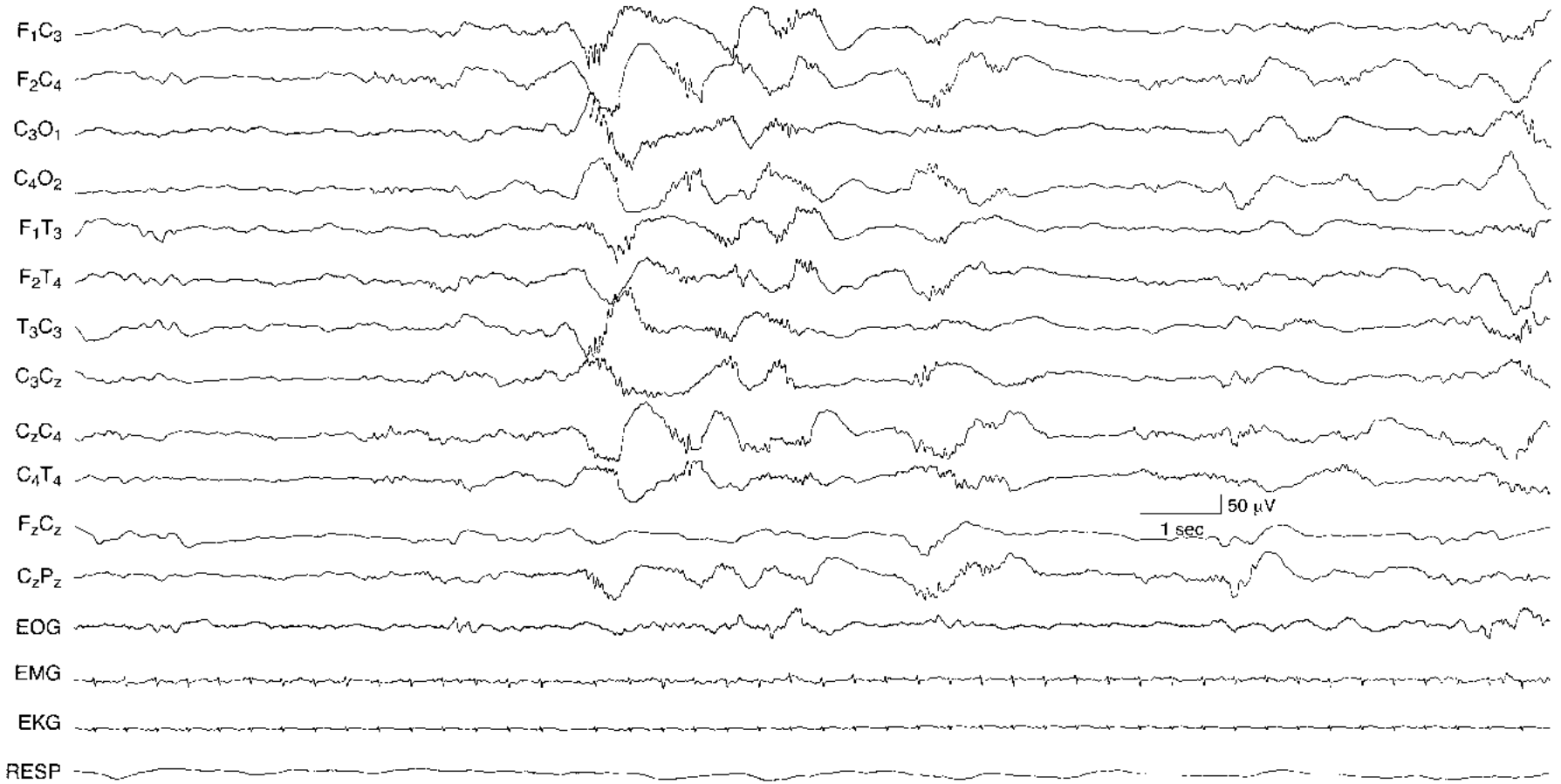

Figure 4.9 29 to 30 weeks CA. Central beta–delta complexes and discontinuity of the background. Beta–delta complexes are present in the central regions bilaterally, but occur asynchronously on the two sides. The background activity is discontinuous with some low-voltage activity superimposed.

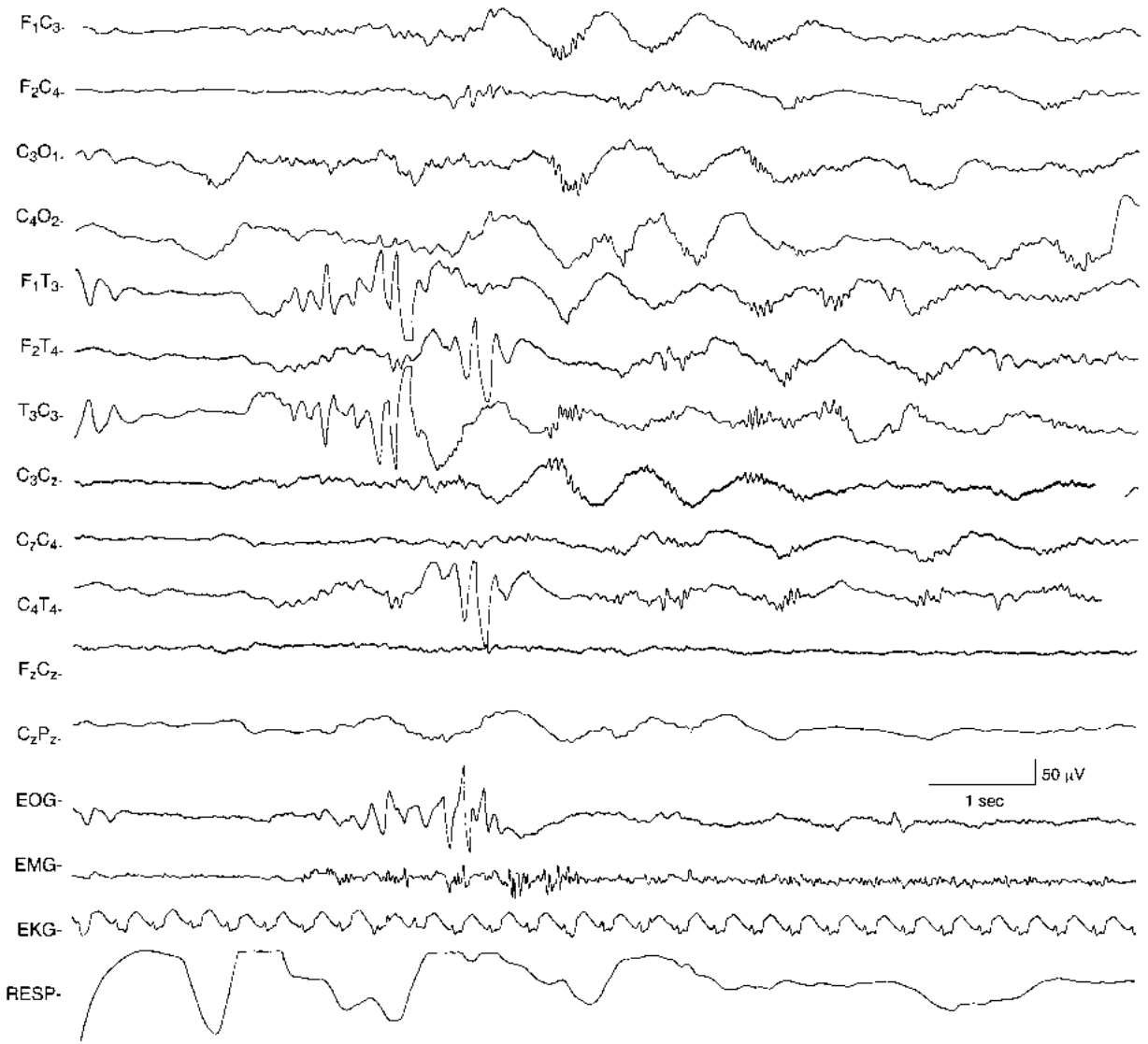

Figure 4.10 29 to 30 weeks CA. Central beta–delta complexes and temporal theta bursts. Theta bursts are present independently on the right and left temporal regions. Beta–delta complexes are present bilaterally, although asynchronous and more prominent on the left.

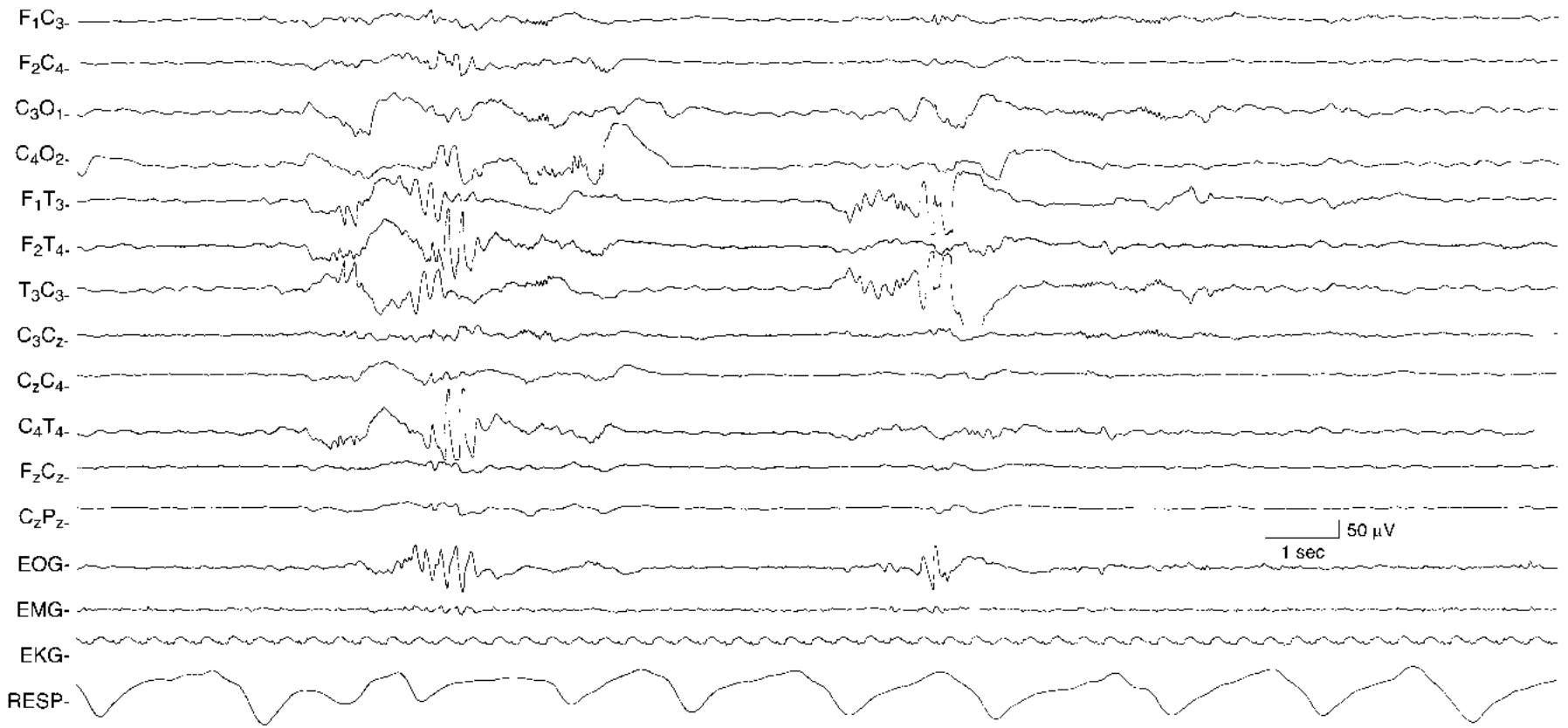

Figure 4.11 29 to 30 weeks CA. Bilateral, independent temporal theta bursts. Temporal theta bursts are present bilaterally, but independently. The background activity is discontinuous. The low-voltage rhythmic slow activity present during periods of quiescence is EKG artifact. This sample is from the same recording in Figure 4.12.

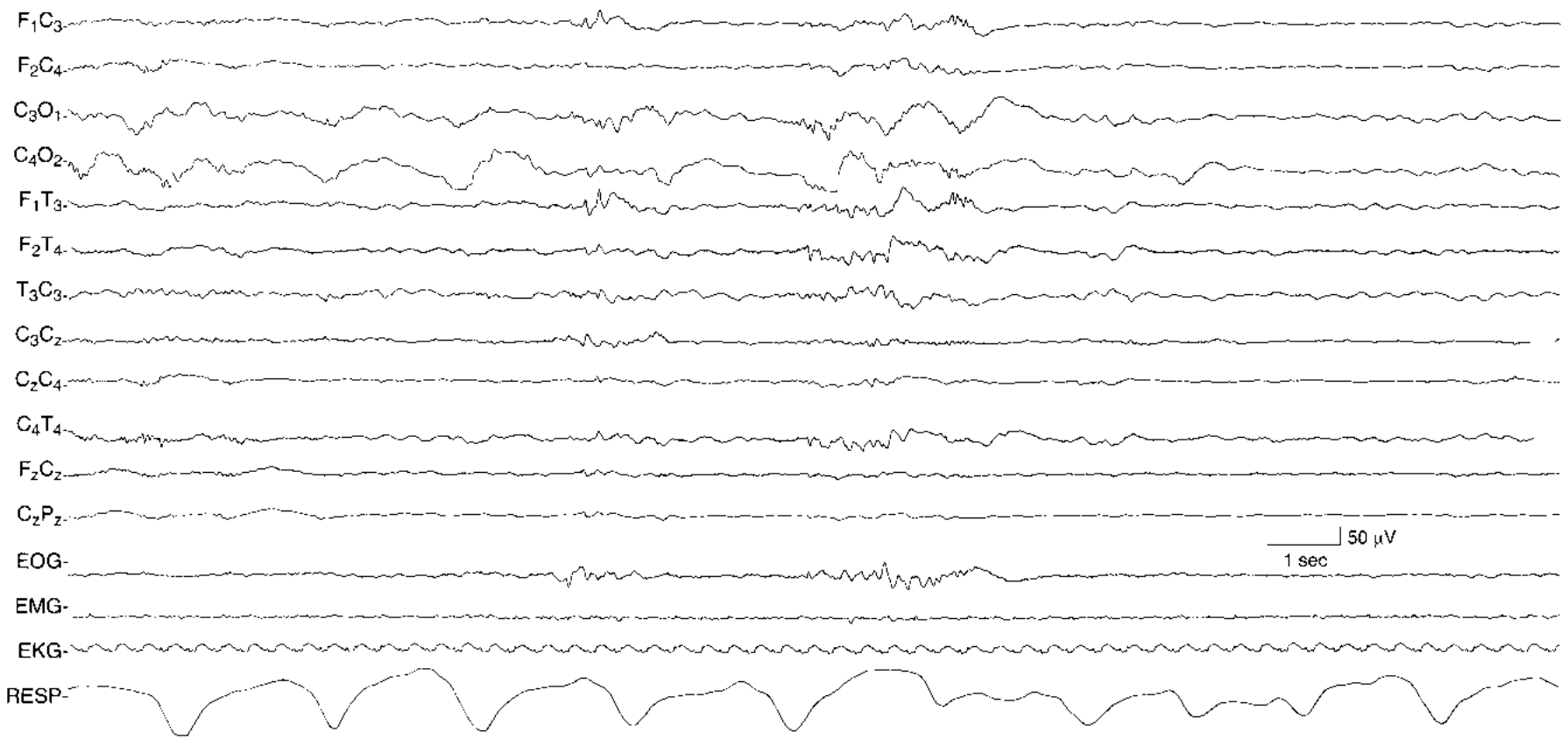

Figure 4.12 29 to 30 weeks CA. Occipital slow activity and central beta–delta complexes. There is moderate voltage, very slow activity in the occipital regions bilaterally in the early portion of the sample. Beta–delta complexes that are more central in location are present later. The recording then becomes discontinuous with EKG artifact superimposed. This sample is from the same recording in Figure 4.11.

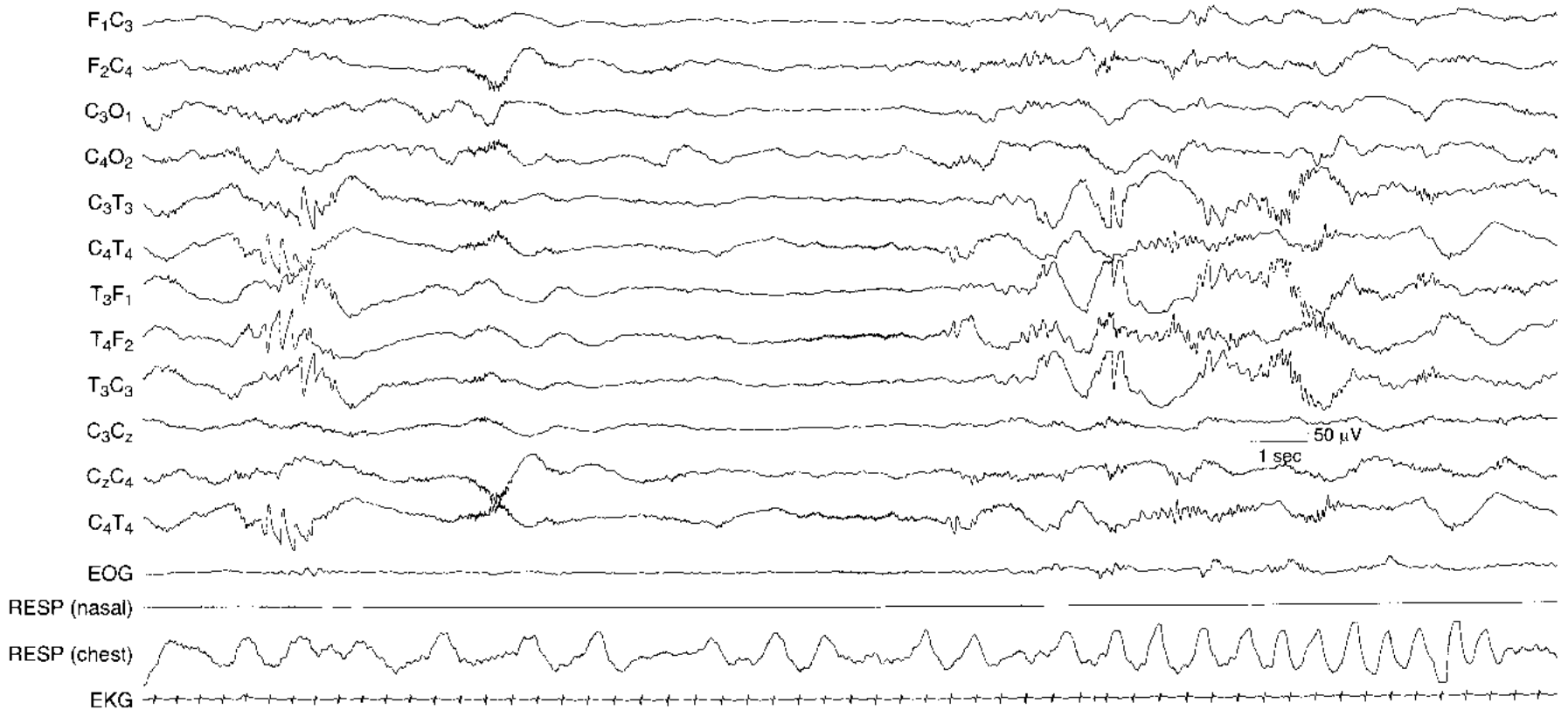

Figure 4.13 30 to 32 weeks CA. Beta–delta complexes in temporal regions and temporal theta bursts. Beta complexes are present in the temporal regions in the latter half of the sample. Earlier there is a beta–delta complex in the right central region. In the initial portion of the sample there are also theta bursts in the temporal regions bilaterally, but asynchronously. The background activity is discontinuous.

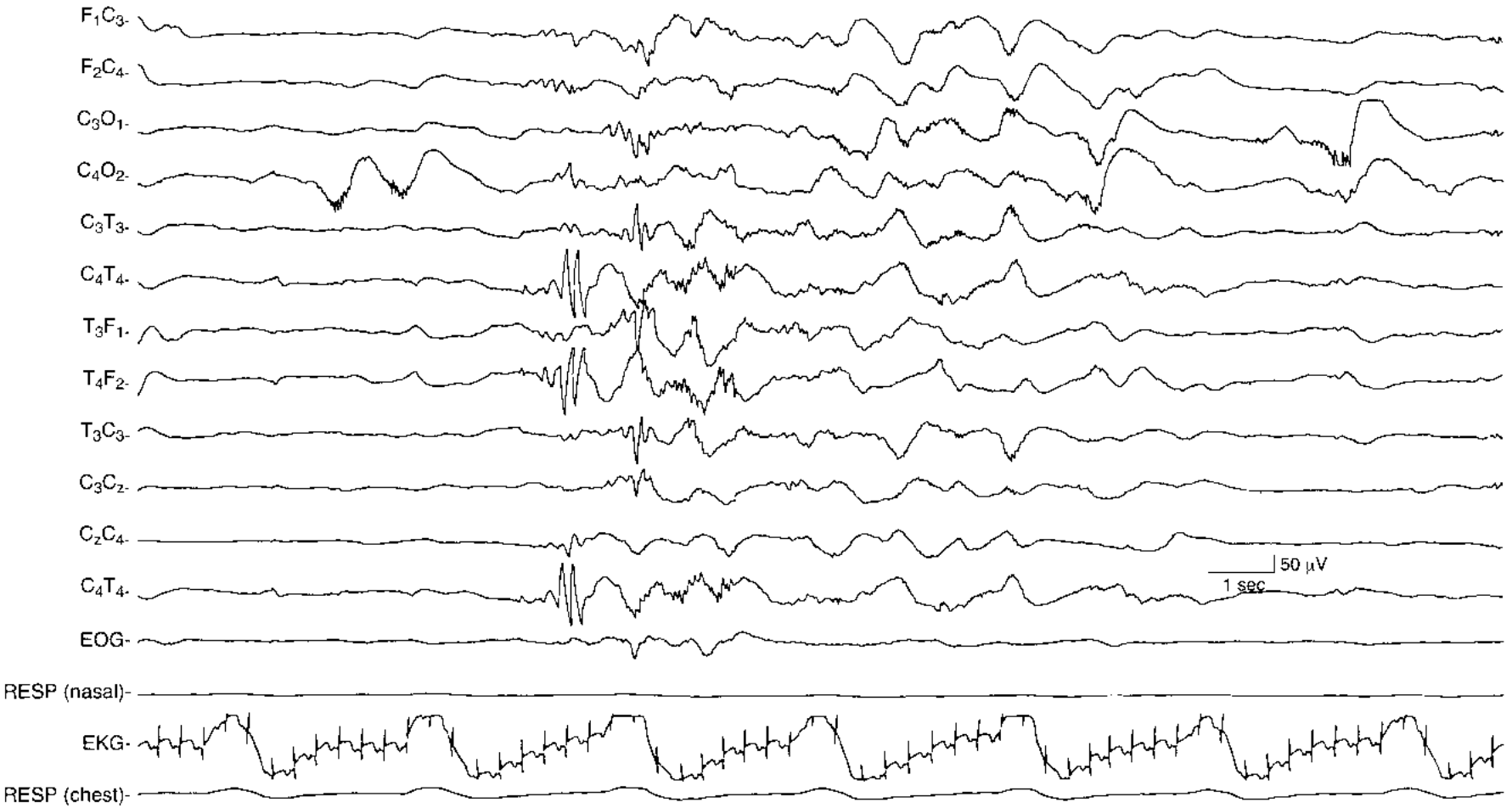

Figure 4.14 30 to 32 weeks CA. Beta–delta complexes in the occipital, temporal, and central regions, and temporal theta bursts. In the early portion of the sample, a beta–delta complex is present in the right occipital region. Then there are bilateral, independent temporal theta bursts. Later, beta–delta complexes are present in the central regions bilaterally. The background activity is discontinuous.

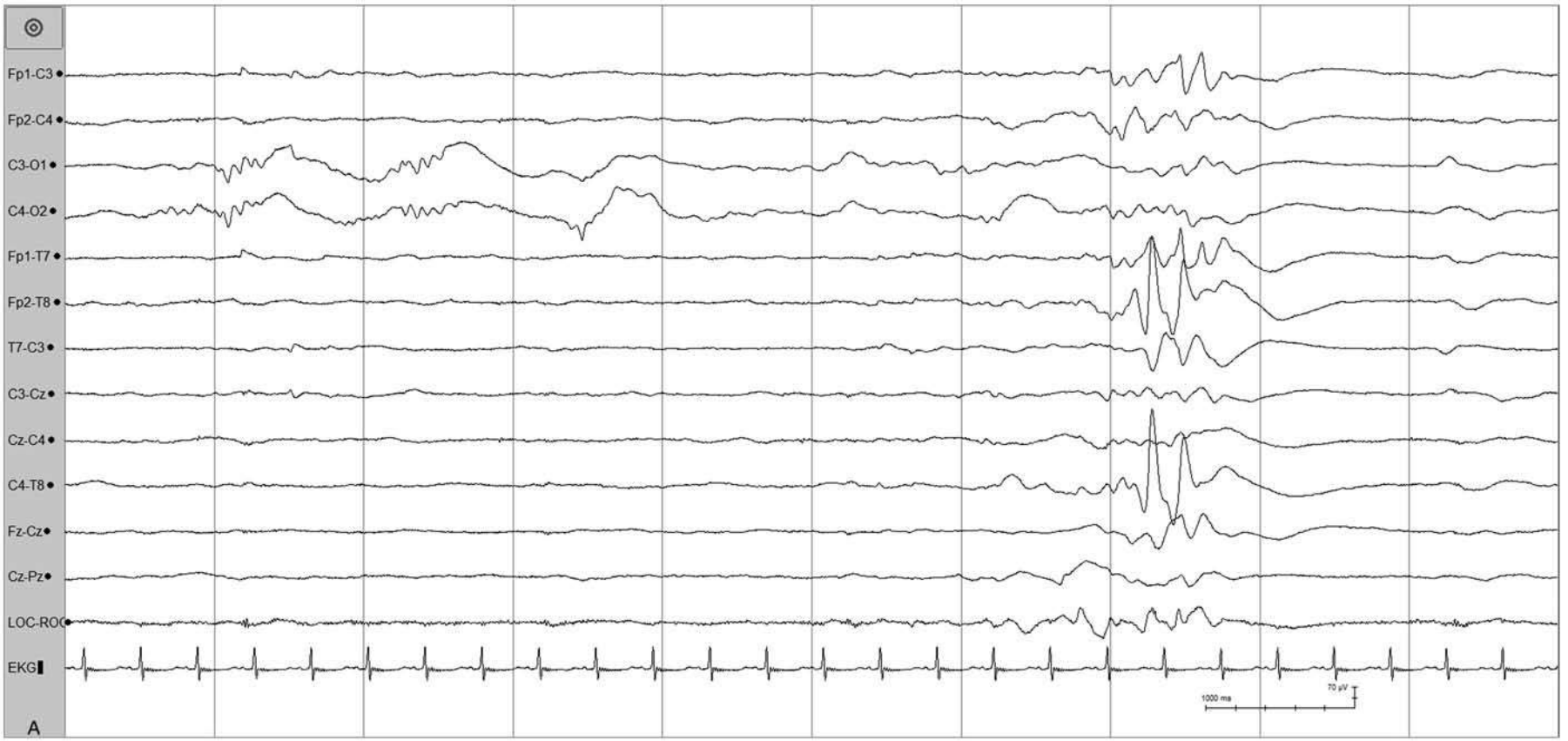

Figure 4.15 (A) and (B) 30 to 32 weeks CA. Extrauterine development of graphoelements. Beta–delta complexes, independent bitemporal bursts, decreased discontinuity, and increased synchrony are present in this 31-week CA infant born at 24 weeks CA and recorded at 7 weeks of life. **(A)** Beta–delta complexes in posterior regions and temporal theta burst on the right. (*continued*)

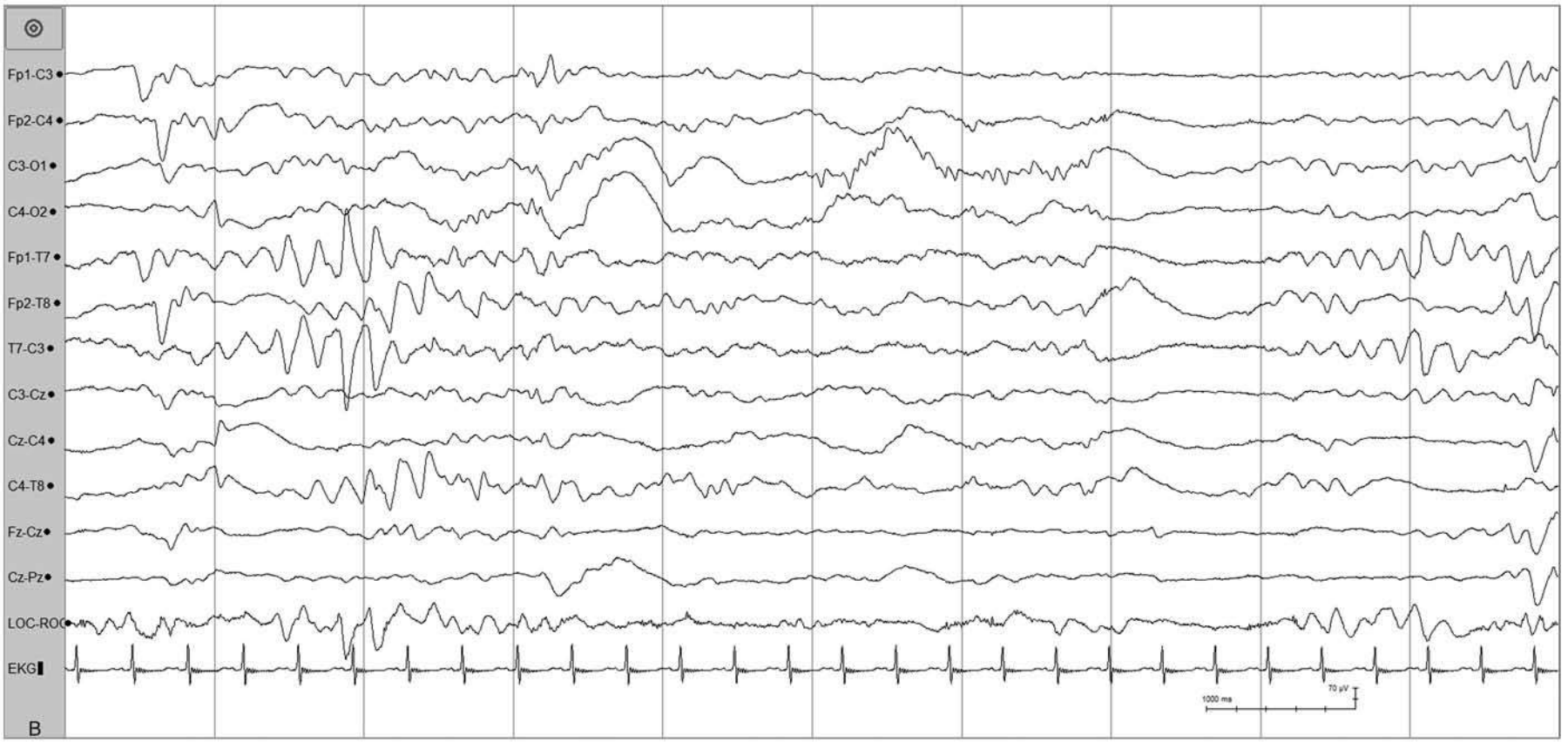

Figure 4.15 (*continued*) **(B)** Temporal theta burst on the left with variable synchrony and continuity.

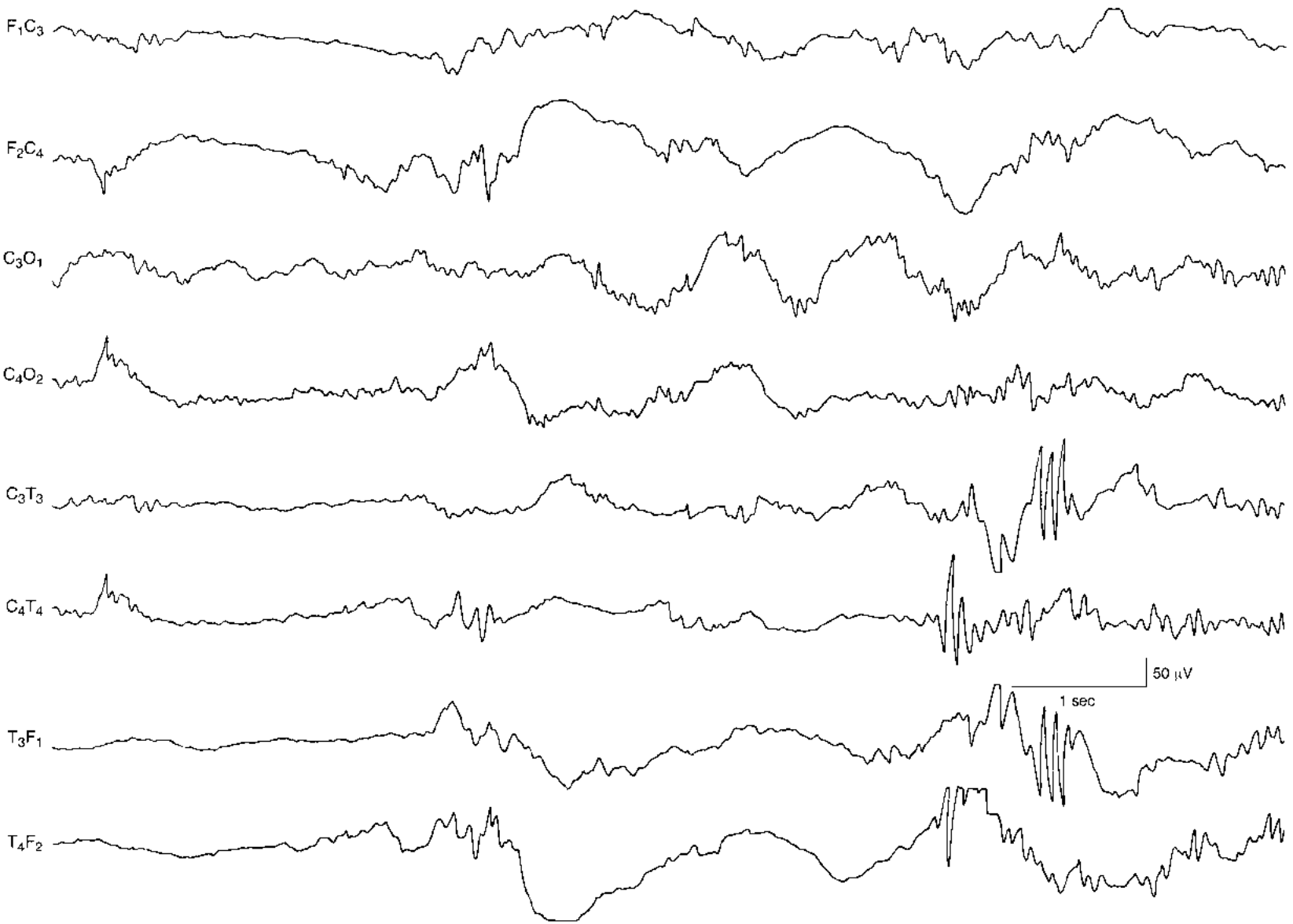

Figure 4.16 33 weeks CA. Bilateral, asynchronous, temporal alpha bursts. Alpha bursts are present in the temporal regions, appearing independently and asynchronously on the two sides.

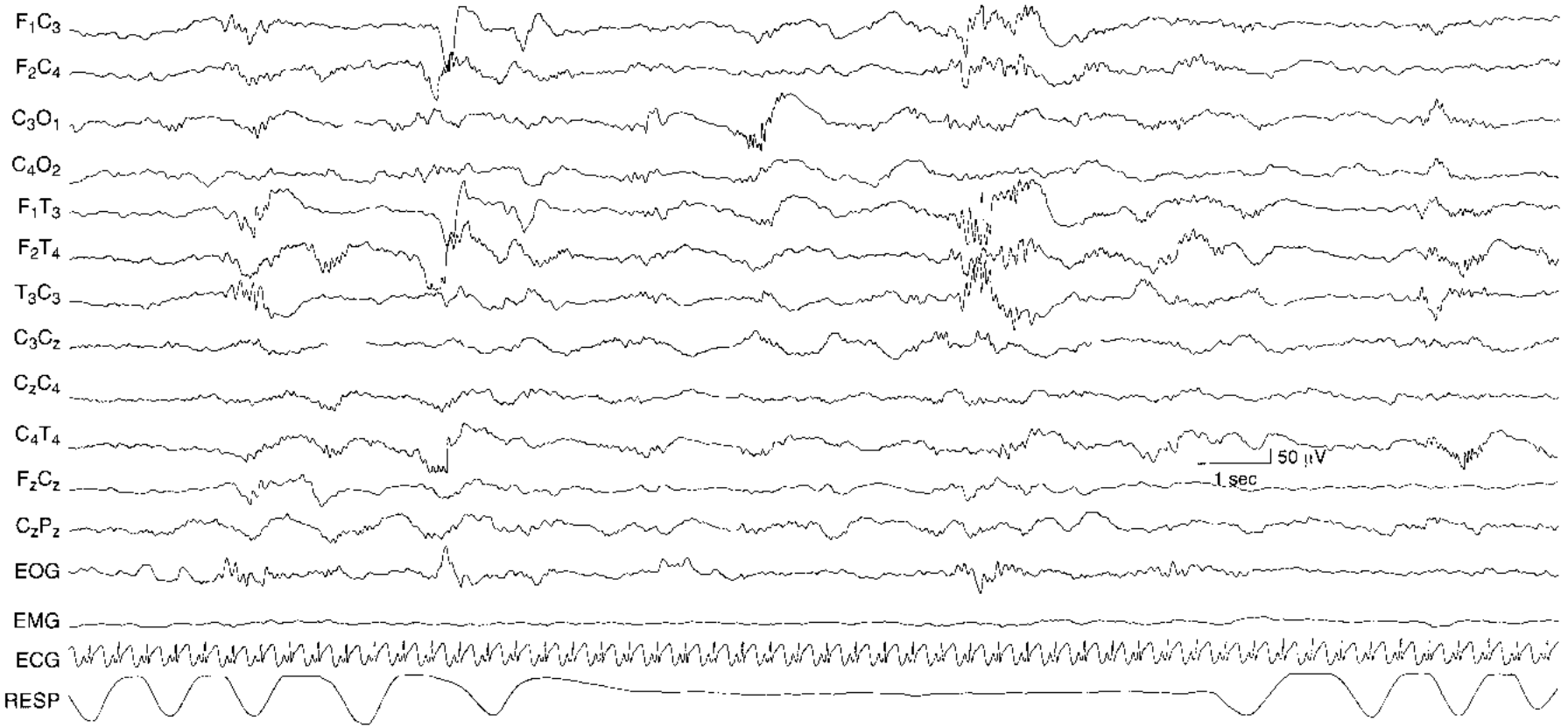

Figure 4.17 33 weeks CA. Temporal alpha burst, occipital beta–delta complexes, and *tracé discontinu*. Temporal bursts with a frequency in the alpha range are present on the left. Beta–delta complexes are most prominent in the occipital region on the right. The background activity is discontinuous, although less so than recordings of infants of a younger conceptional age.

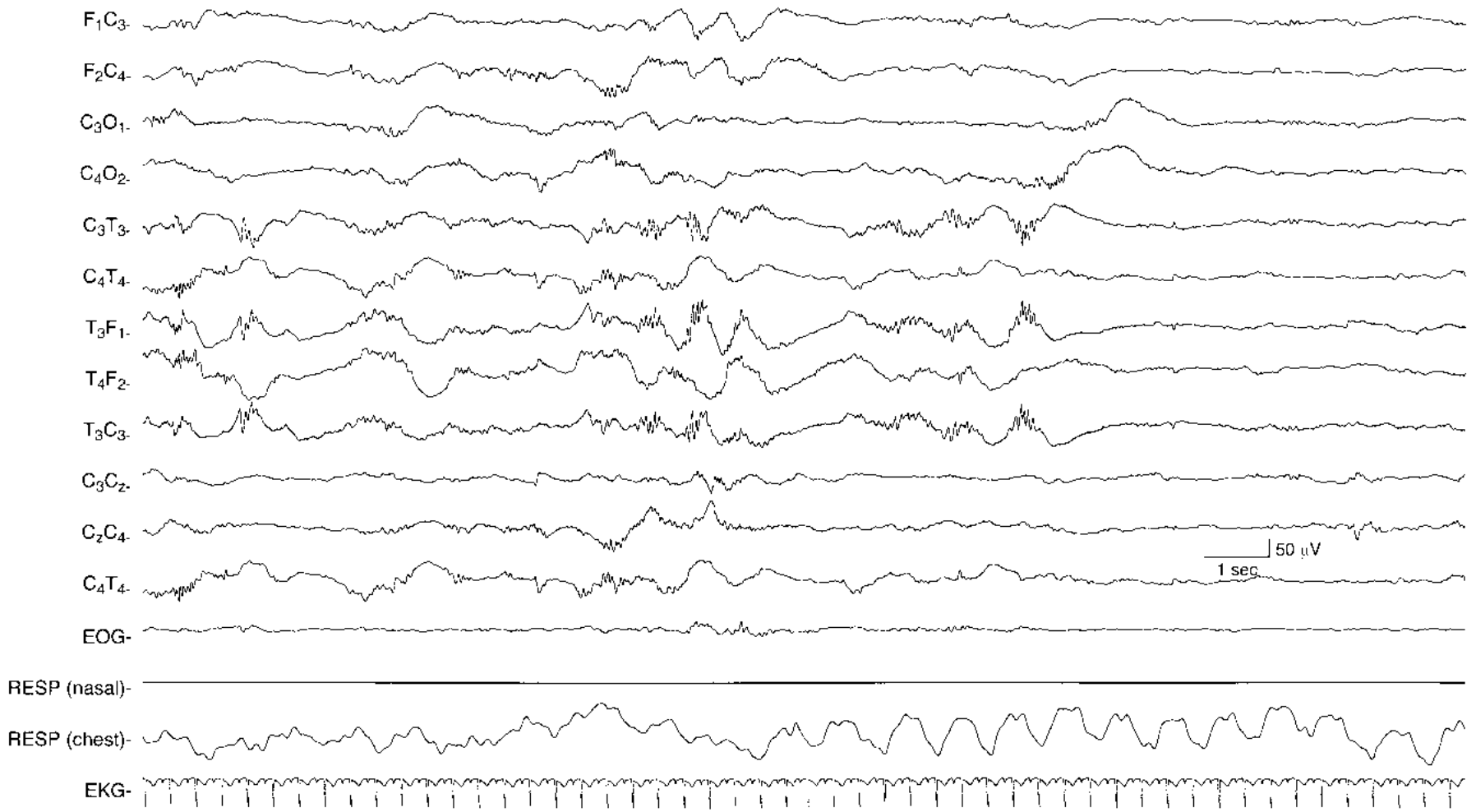

Figure 4.18 33 weeks CA. Beta–delta complexes in the temporal regions. Beta–delta complexes are present in the temporal regions, greater on the left. There is a brief run of alpha frequency activity in the left temporal region early in the sample. The background activity is discontinuous. Periods of discontinuity are shorter and the periods of bursting activity are longer than in infants with a younger conceptional age.

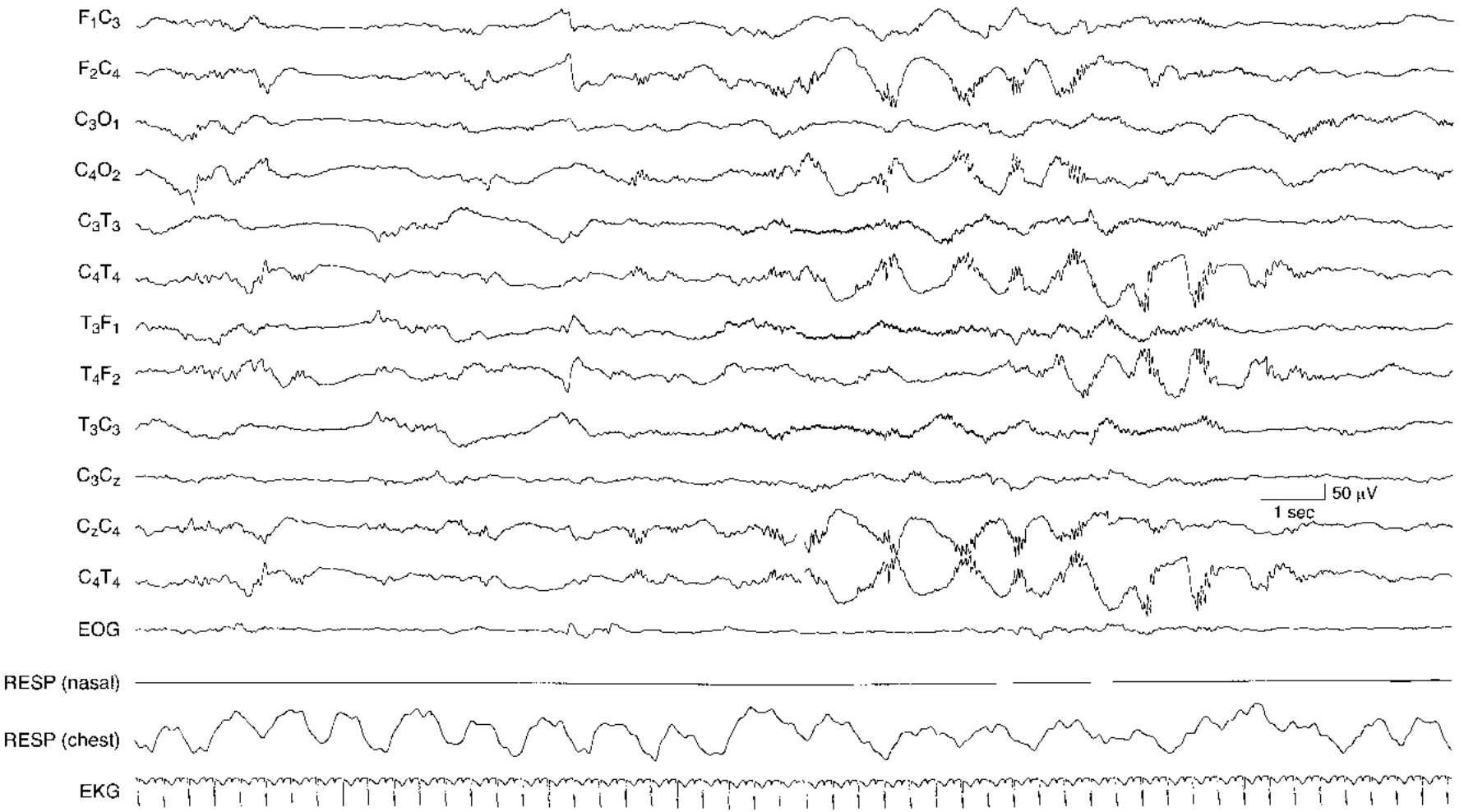

Figure 4.19 34 to 35 weeks CA. Beta–delta complexes in the central and temporal regions and frontal sharp transients. Beta–delta complexes are present in the right central region followed by beta–delta complexes in the right temporal region. There are rudimentary frontal sharp transients, higher in amplitude and more well formed on the right side in the early portion of the sample that suggests that the CA of this infant is early in the 34- to 35-week epoch.

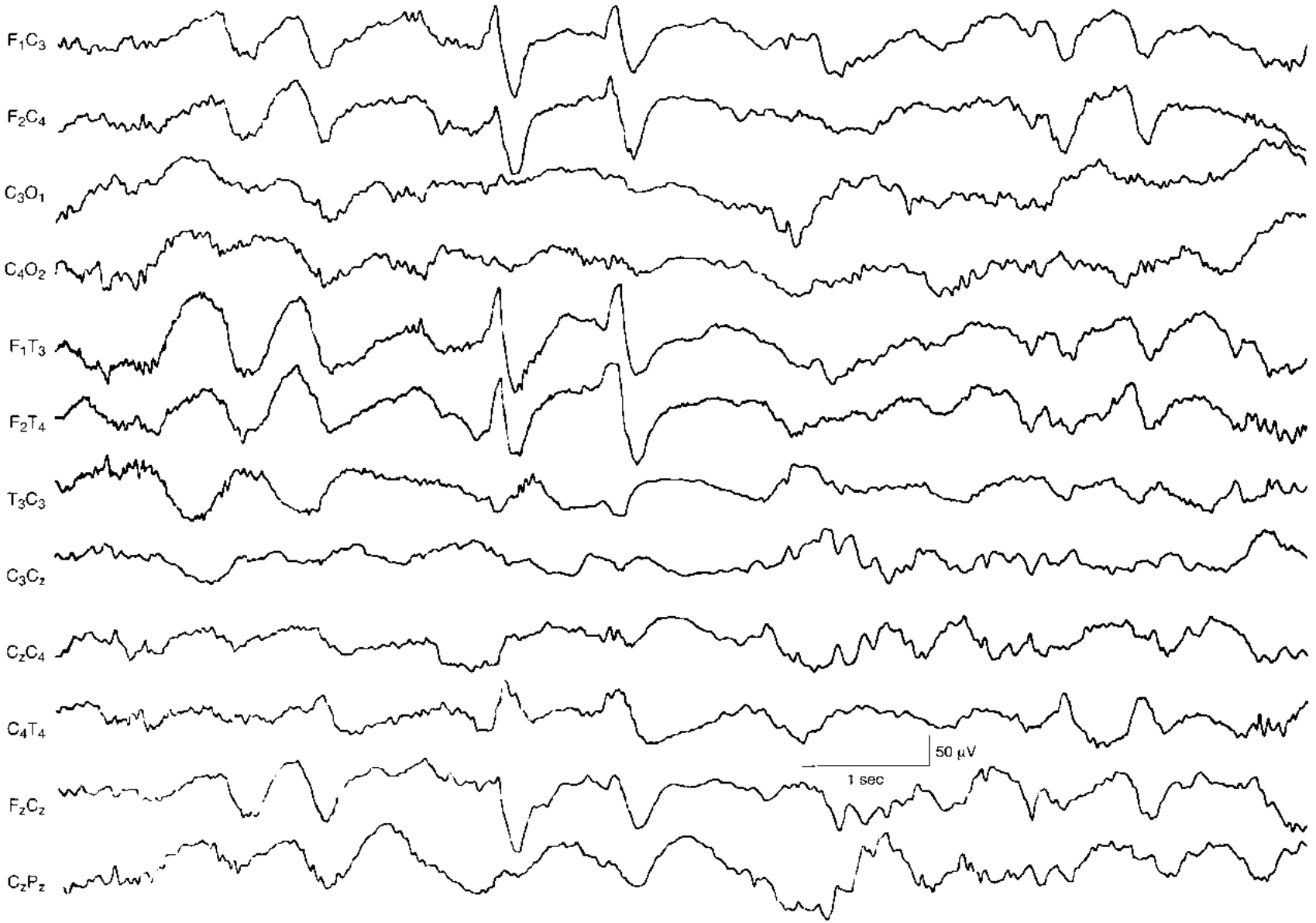

Figure 4.20 34 to 35 weeks CA. Frontal sharp transients. Bilateral, synchronous frontal sharp transients are present in the frontal leads bilaterally.

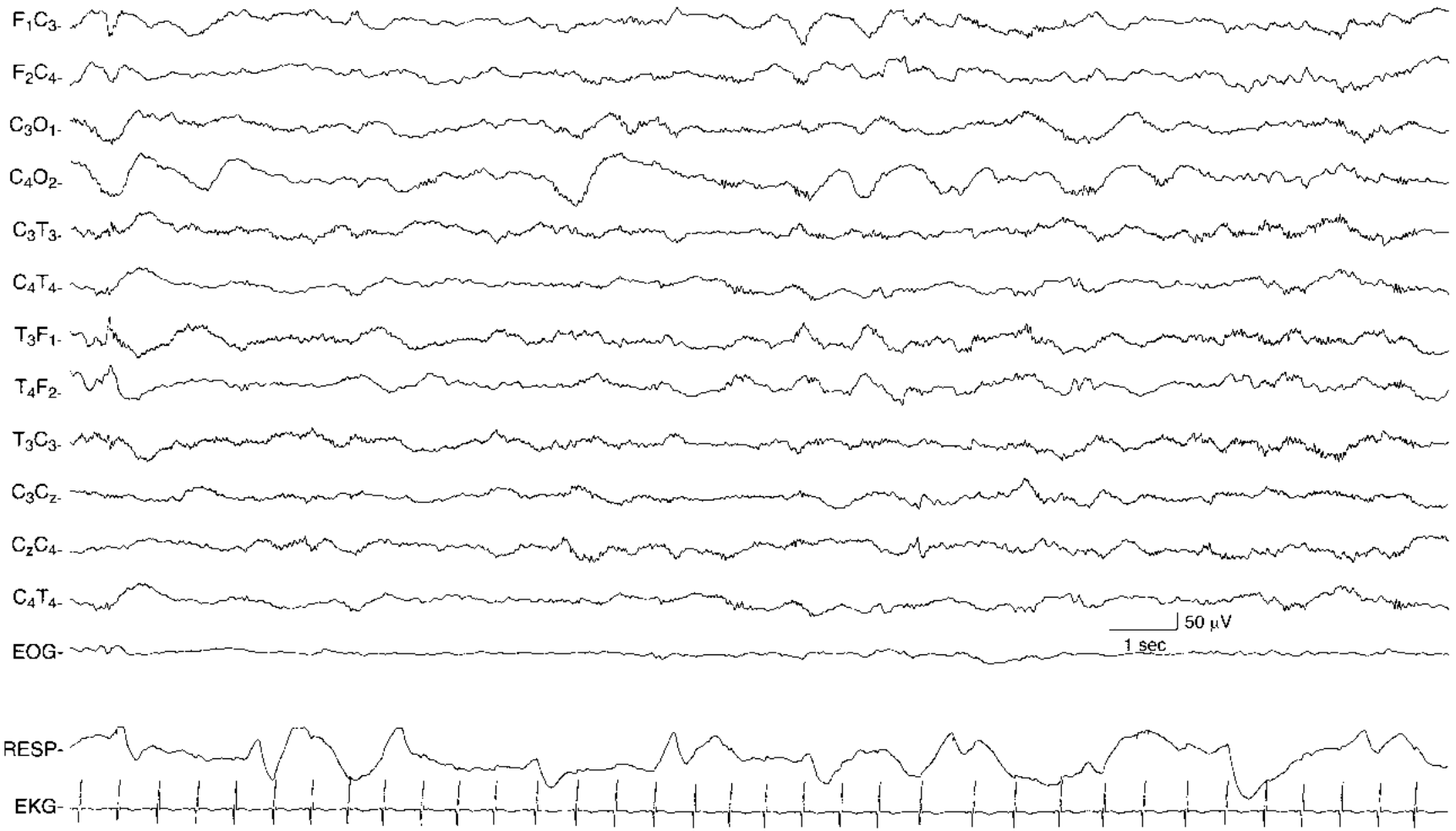

Figure 4.21 34 to 35 weeks CA. Awake: relative continuous background activity with some interhemispheric asynchrony. The background activity is continuous with intermittent beta–delta complexes in the occipital regions. This sample is from the same recording of the infant in Figure 4.22.

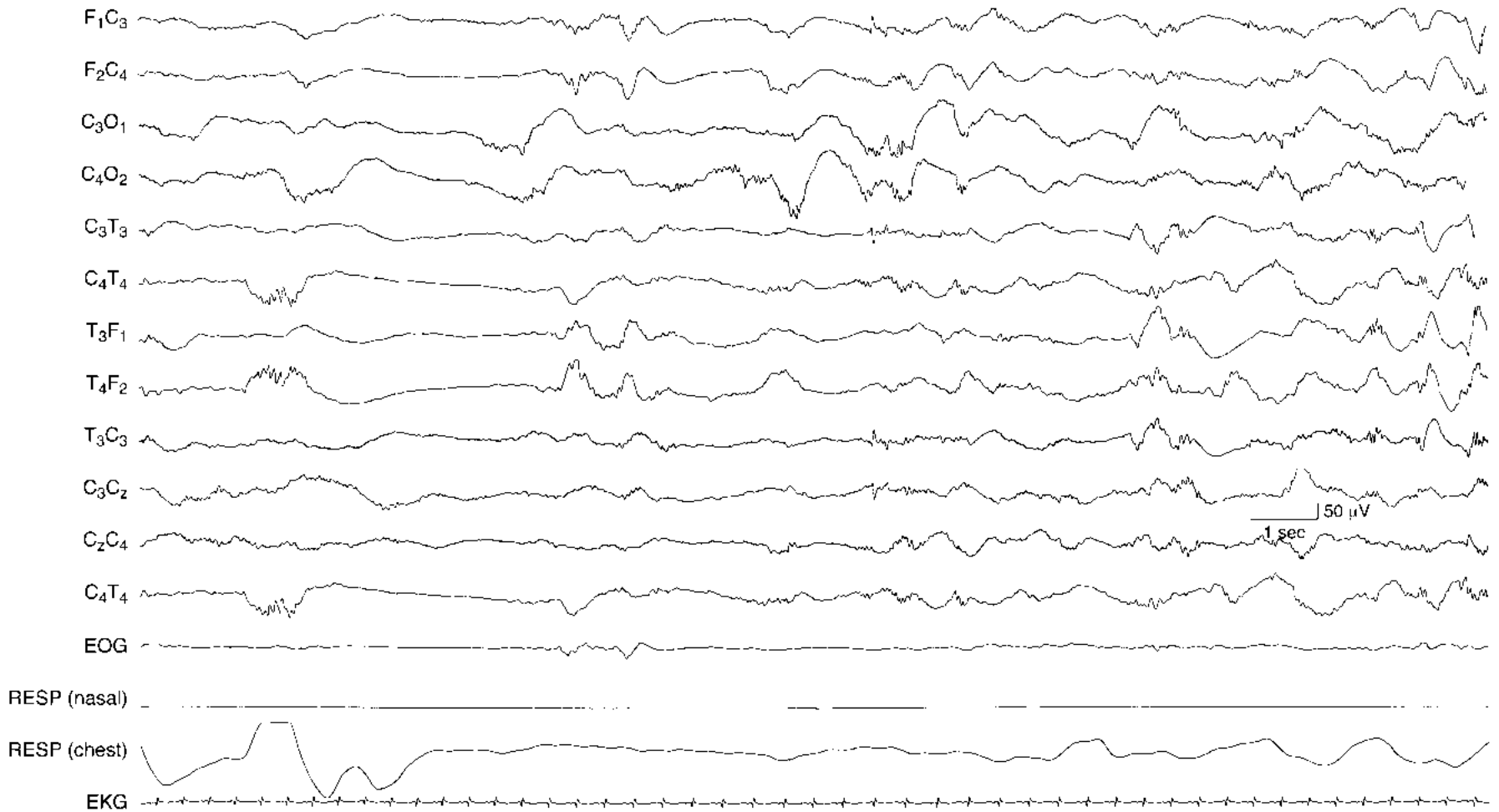

Figure 4.22 34 to 35 weeks CA. NREM (quiet) sleep: discontinuous background activity. There is a period of discontinuity similar to other periods of discontinuity in the same recording during this stage of sleep. This sample is from the same recording of the infant in Figure 4.21.

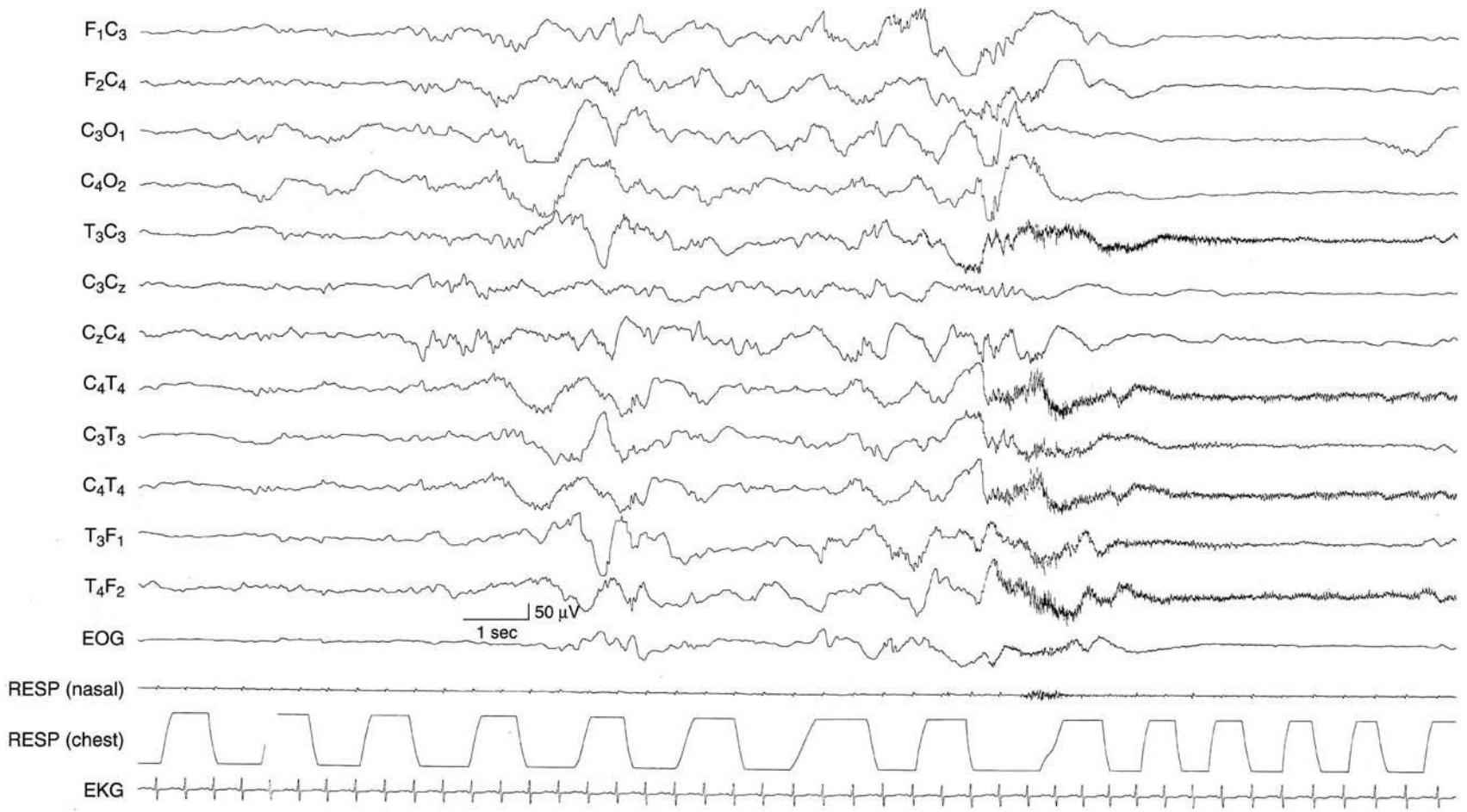

Figure 4.23 36 to 37 weeks CA. Arousal from NREM (quiet) sleep: generalized voltage attenuation associated with clinical arousal. The early portion of the sample demonstrates the discontinuity of NREM (quiet) sleep. The infant then self-arouses. This is associated with generalized voltage attenuation (and EMG artifact from the temporal muscles).

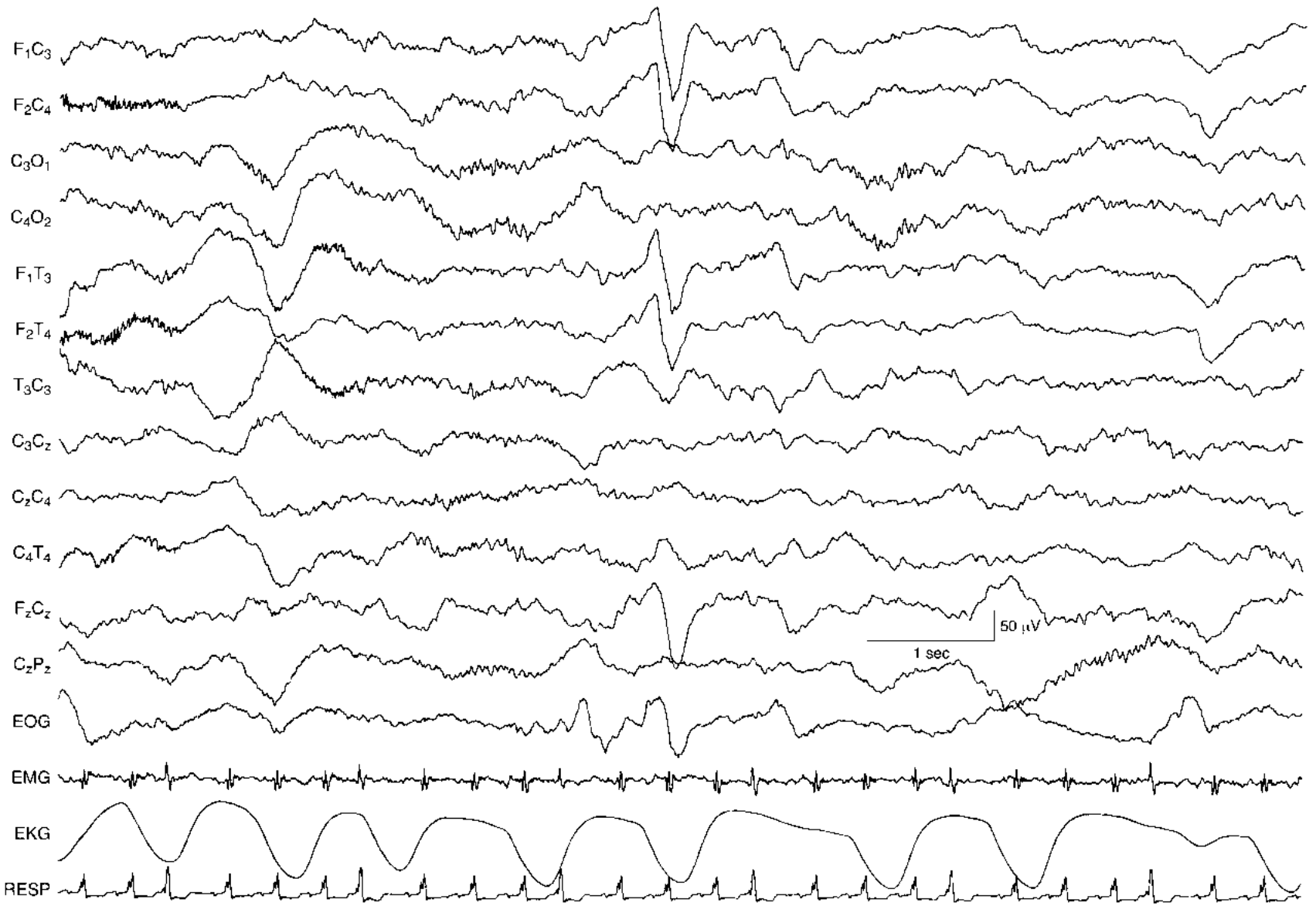

Figure 4.24 36 to 37 weeks CA. Frontal sharp transients, continuous polyfrequency activity, and a paucity of beta–delta complexes. Frontal sharp transients occur synchronously and symmetrically on the two sides. The background activity is relatively continuous with polyfrequency activity throughout.

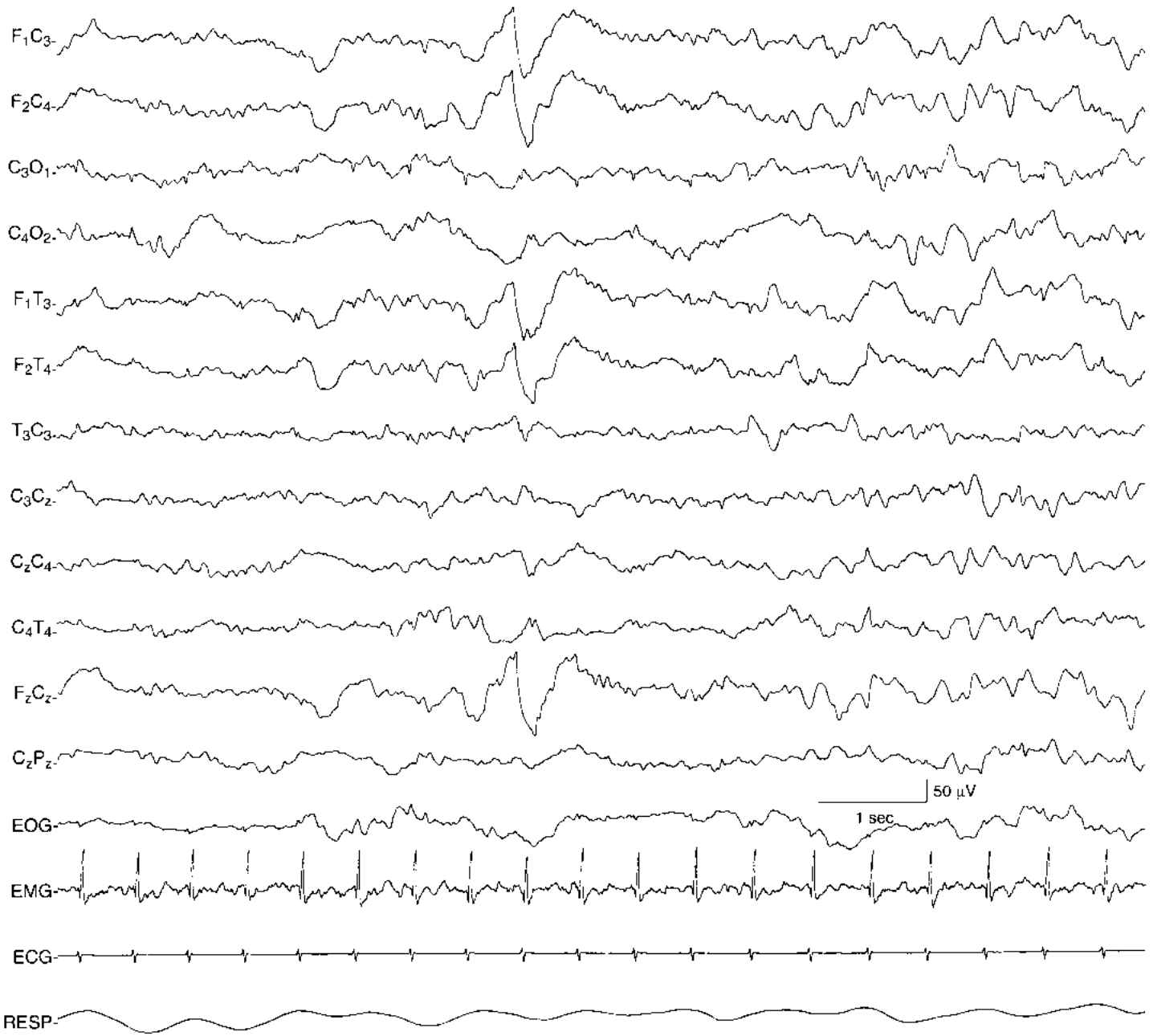

Figure 4.25 38 to 40 weeks CA. Frontal sharp transients with continuous background activity. Bilateral, synchronous, frontal sharp transients are present. They occur randomly. Their occurrence is similar to those of earlier conceptional ages when they first emerge as developmental landmarks, but at this CA frontal sharp transients occur with continuous background activity.

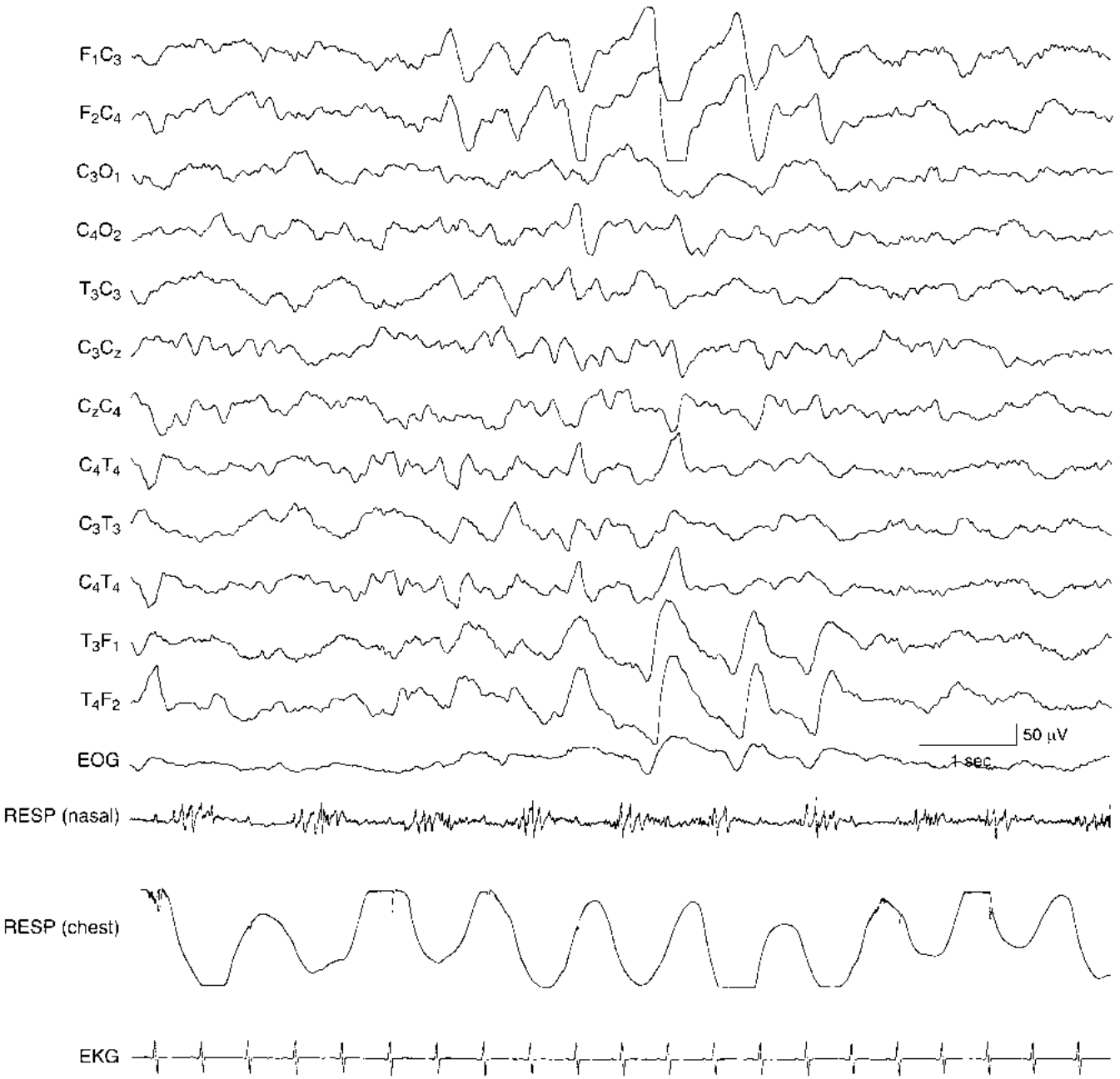

Figure 4.26 38 to 40 weeks CA. Repetitive frontal sharp transients. As at younger CAs, frontal sharp transients may occur in brief runs.

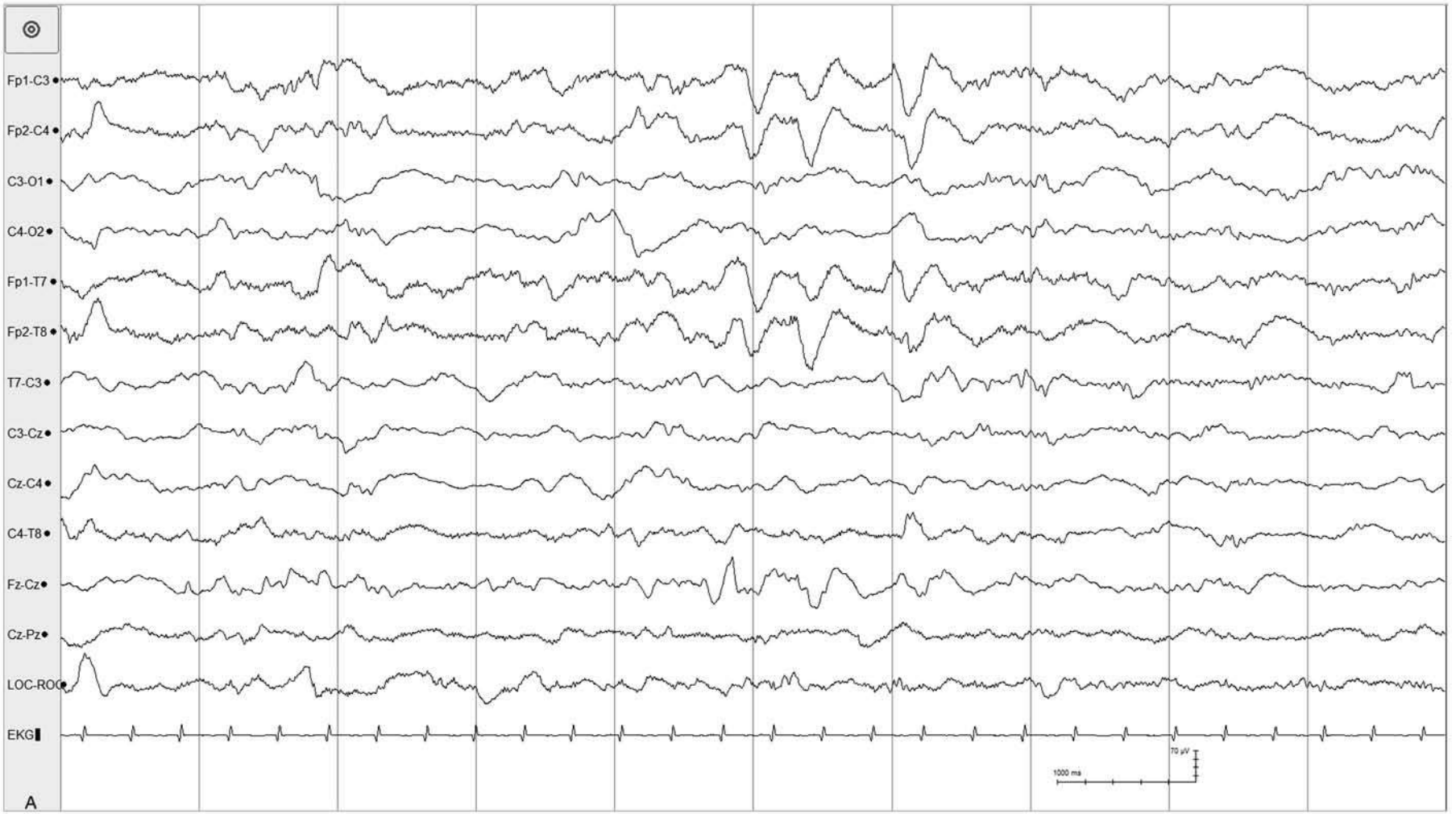

Figure 4.27 (A) and (B) 38 to 40 weeks CA. Symmetrical and asymmetrical frontal sharp transients. (A) Brief run of frontal sharp transients in a 38-week CA infant. (*continued*)

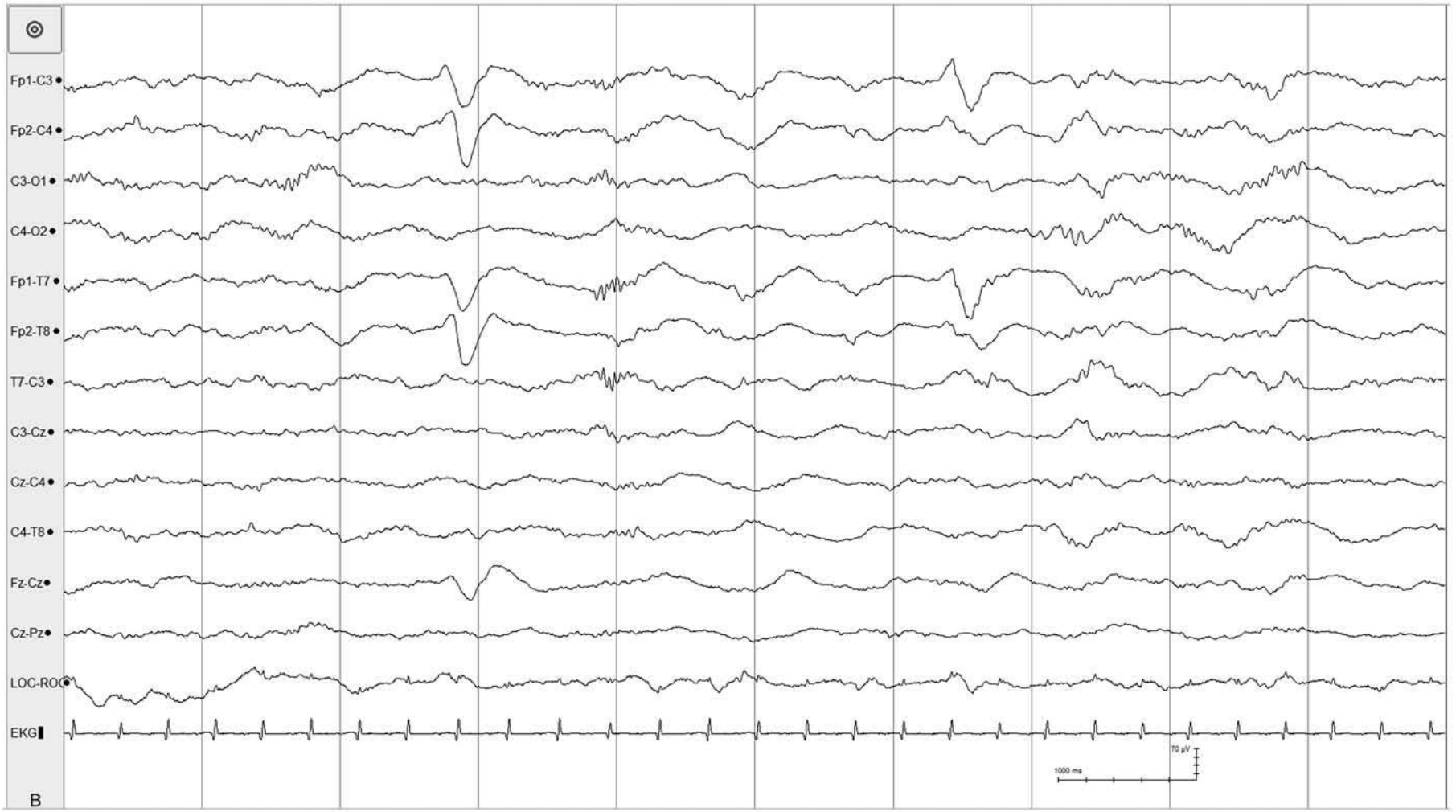

Figure 4.27 (*continued*) **(B)** Both symmetric and asymmetrical frontal sharp transients in the same infant.

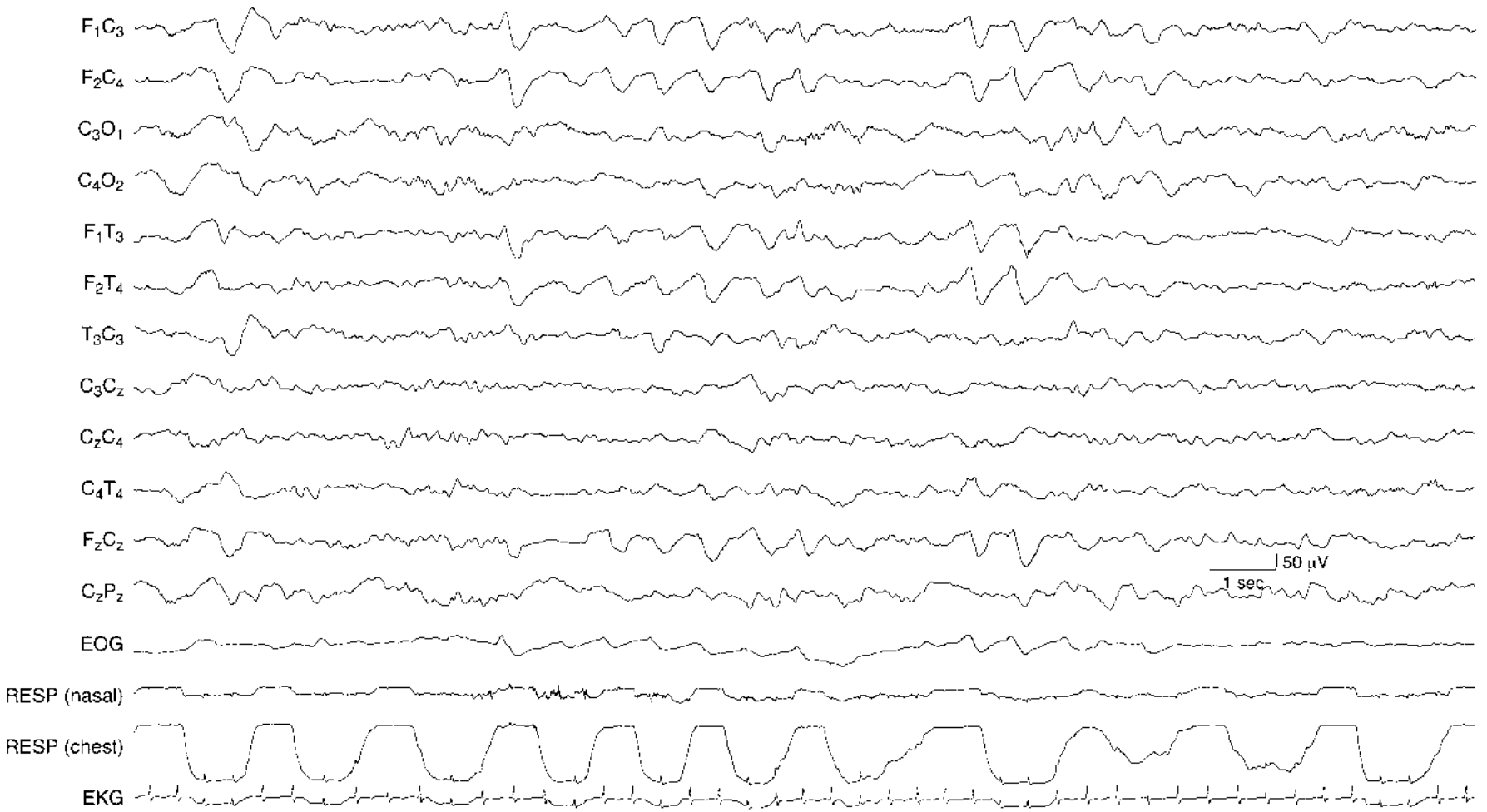

Figure 4.28 38 to 40 weeks CA. Rhythmic bifrontal delta activity in transitional sleep. There is intermittent bifrontal delta activity that, at times, is mixed with frontal sharp transients. Bifrontal delta activity is not a developmental landmark, per se, but this activity is considered a normal variation typically occurring in transitional or indeterminant sleep.

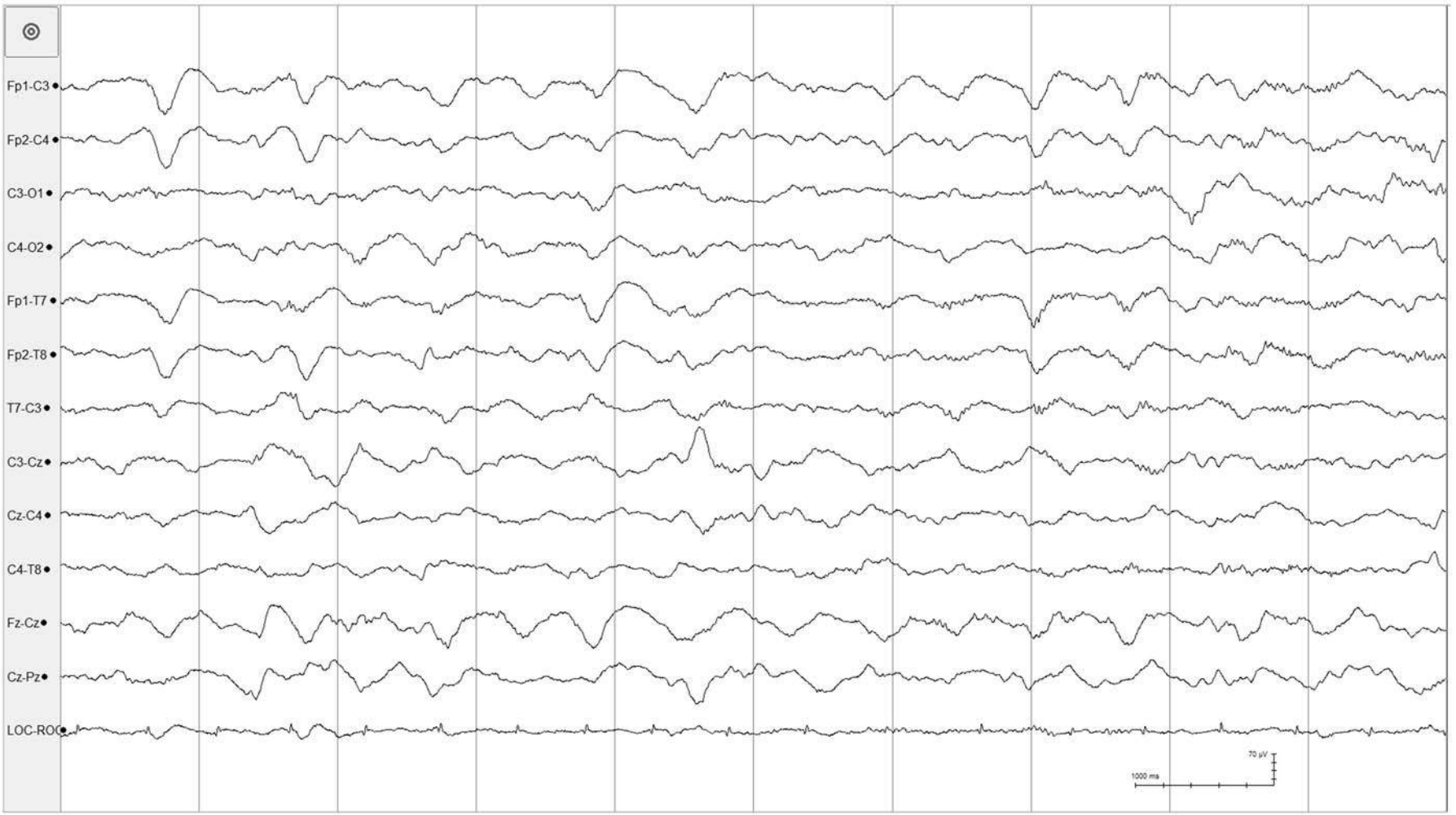

Figure 4.29 38 to 40 weeks CA. Intermittent bifrontal delta activity. Intermittent bifrontal delta activity with occasional frontal sharp transients is present in this 40-week CA infant with other normal features of the EEG.

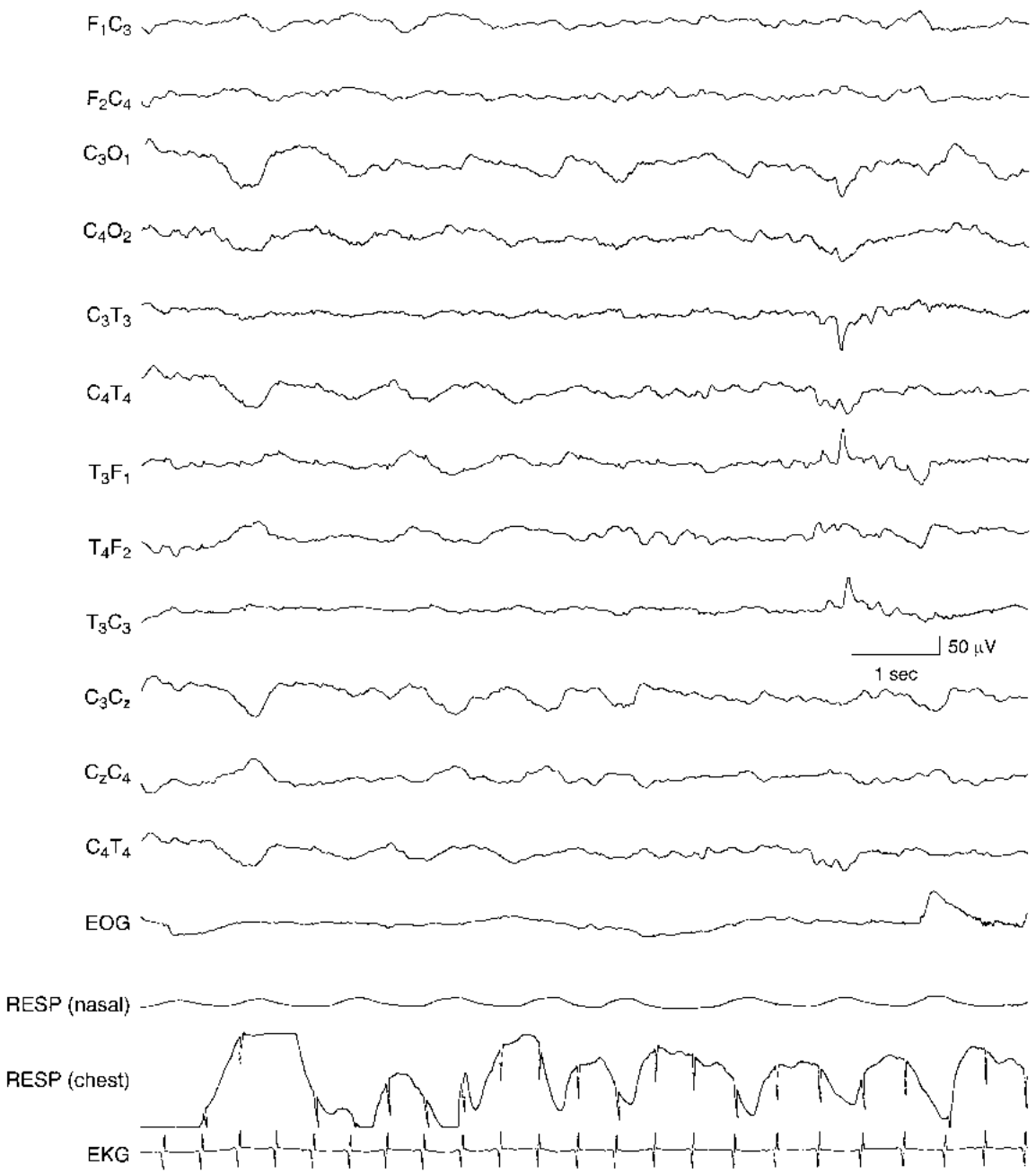

Figure 4.30 38 to 40 weeks CA. Temporal sharp waves. There is a moderate voltage sharp wave in the left temporal region that occurs in isolation. The background activity is normal for CA. Randomly occurring, moderate voltage sharp waves do occur in the EEGs that are otherwise normal and in neonates who also are normal. There is a continuum of the degree of normality to abnormality of these waveforms that is discussed in Chapter 5. This sample is presented to indicate that some temporal sharp waves can be considered normal although the presence of temporal sharp waves does not constitute a developmental landmark.

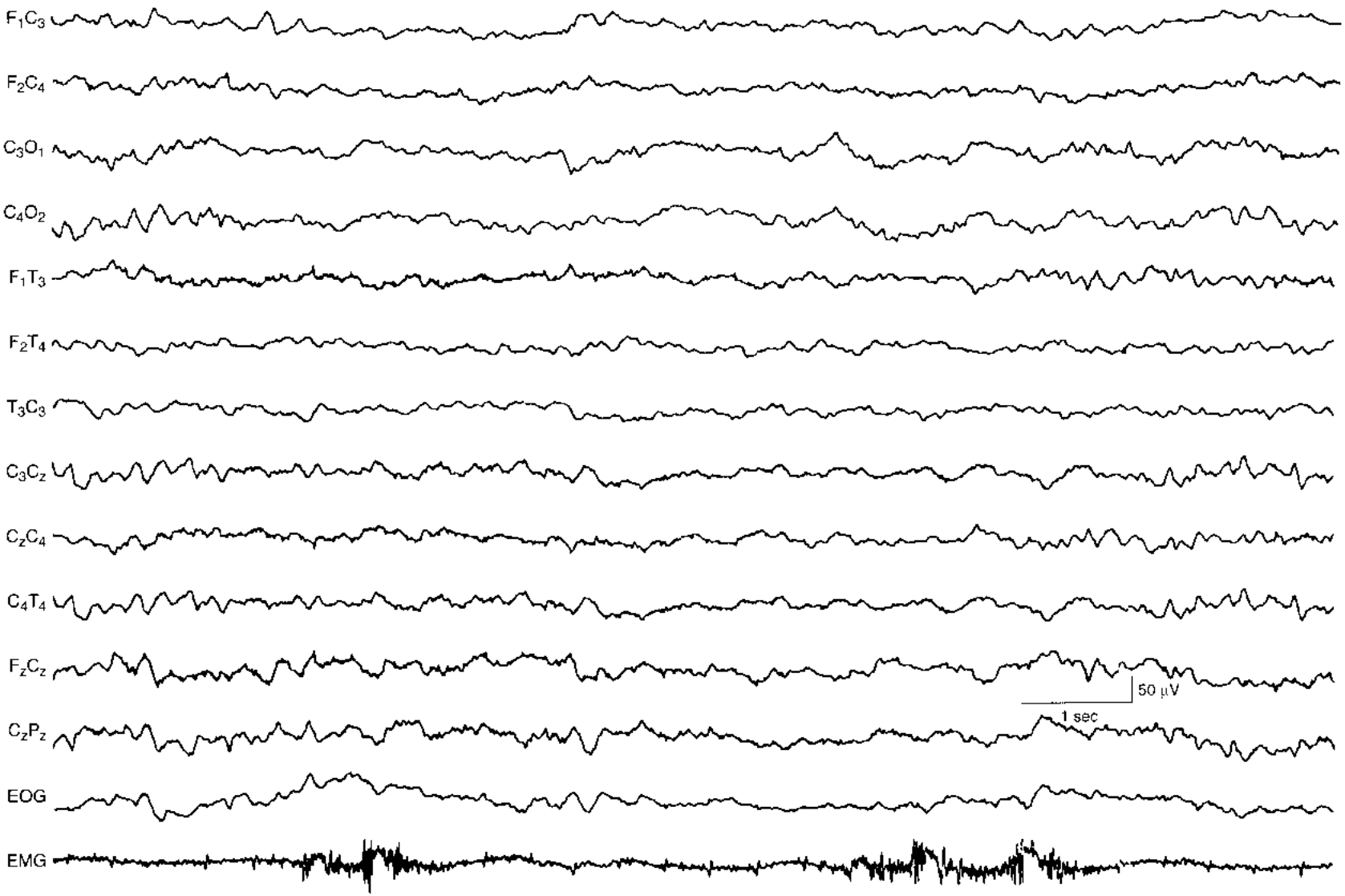

Figure 4.31 38 to 40 weeks CA. Awake: continuous, synchronous polyfrequency activity. There is continuous and synchronous polyfrequency activity that includes a mixture of alpha, beta, theta, and delta activity. (Hrachovy, 2000, with permission.)

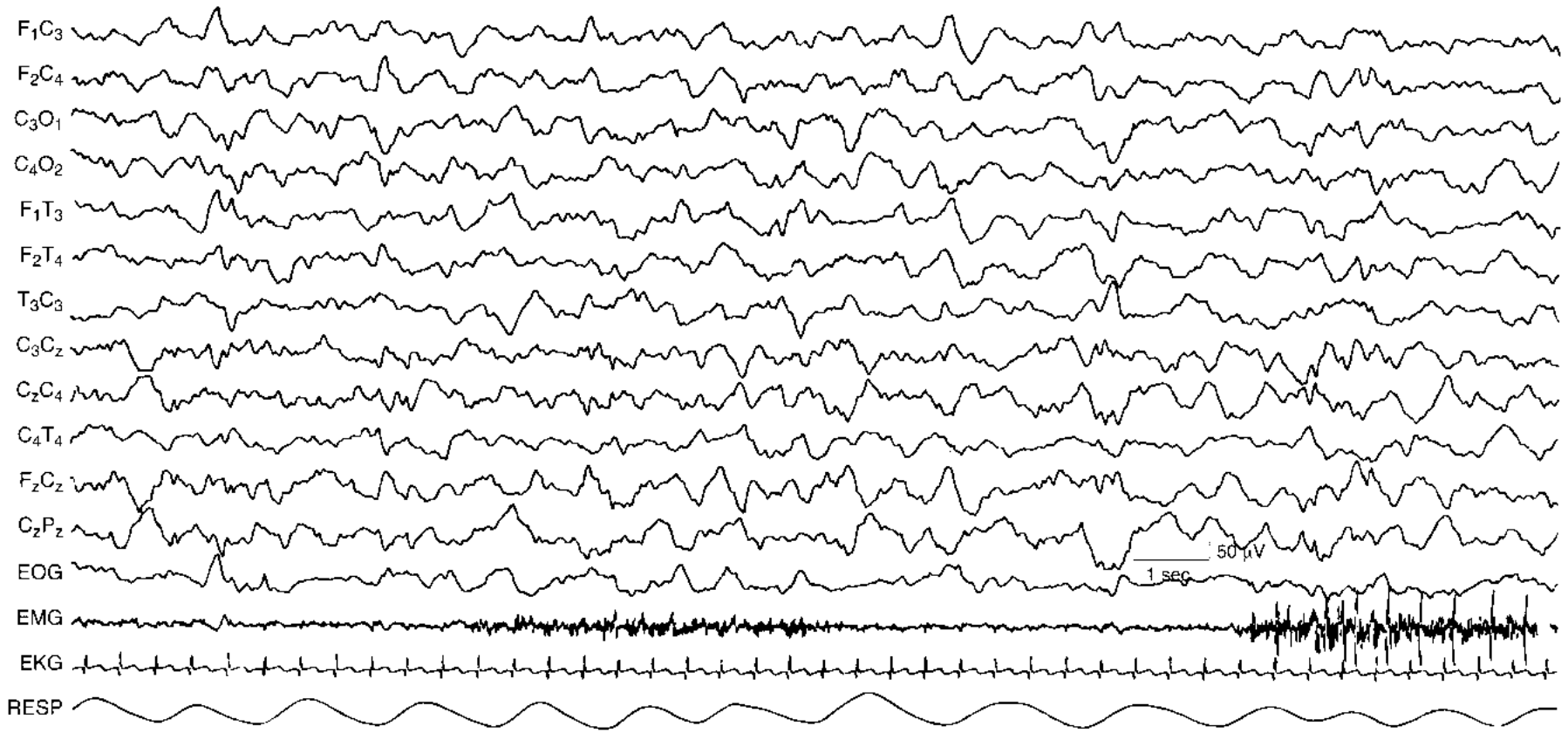

Figure 4.32 38 to 40 weeks CA. NREM (quiet) sleep: continuous slow activity. There is continuous, relatively slow activity that is synchronous on the two sides. Respiration is regular and there are no REMs. (Hrachovy, 2000, with permission.)

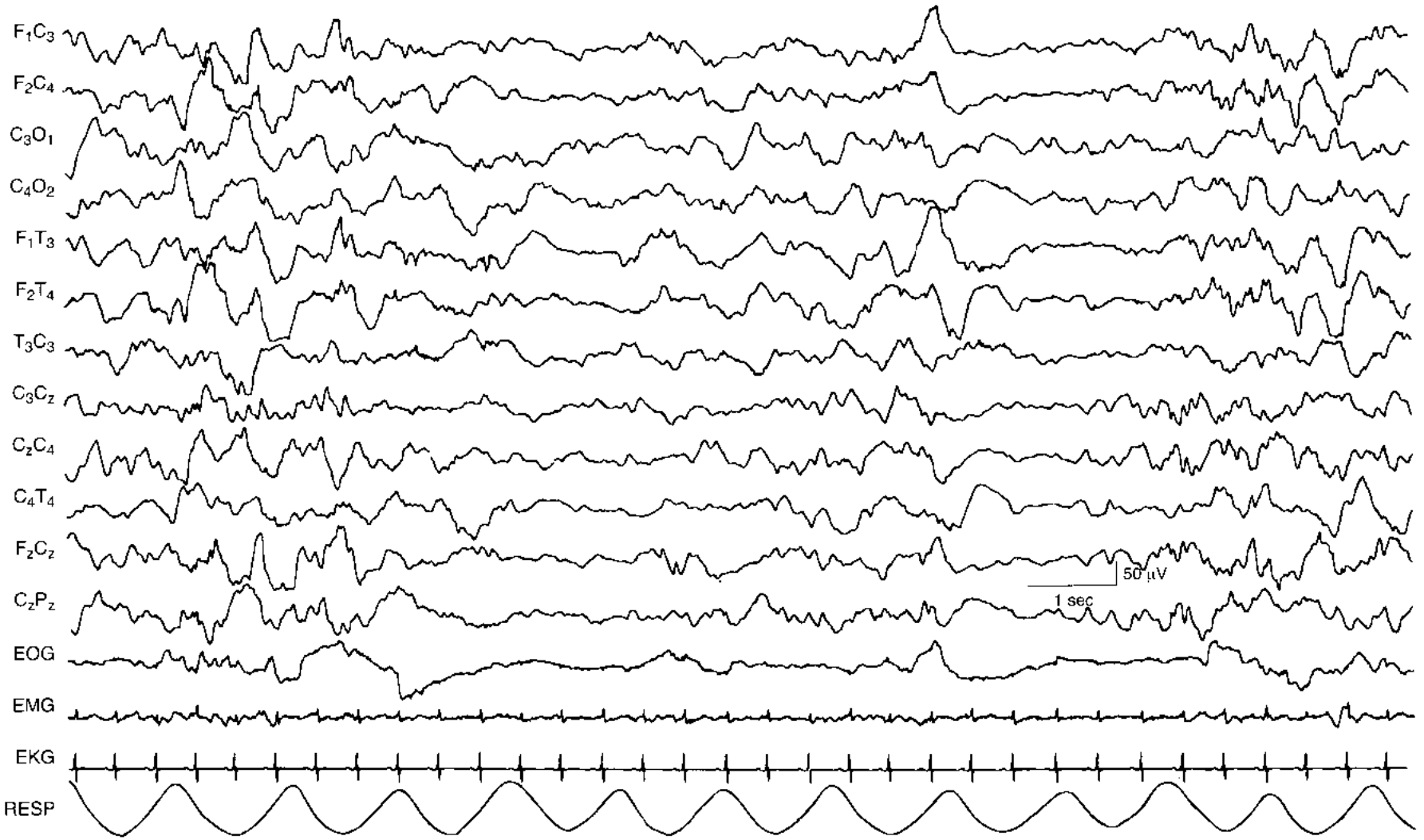

Figure 4.33 38 to 40 weeks CA. *Tracé alternant* in deep NREM (quiet) sleep. There are periods of discontinuity during deep NREM. (Hrachvoy, 2000, with permission.)

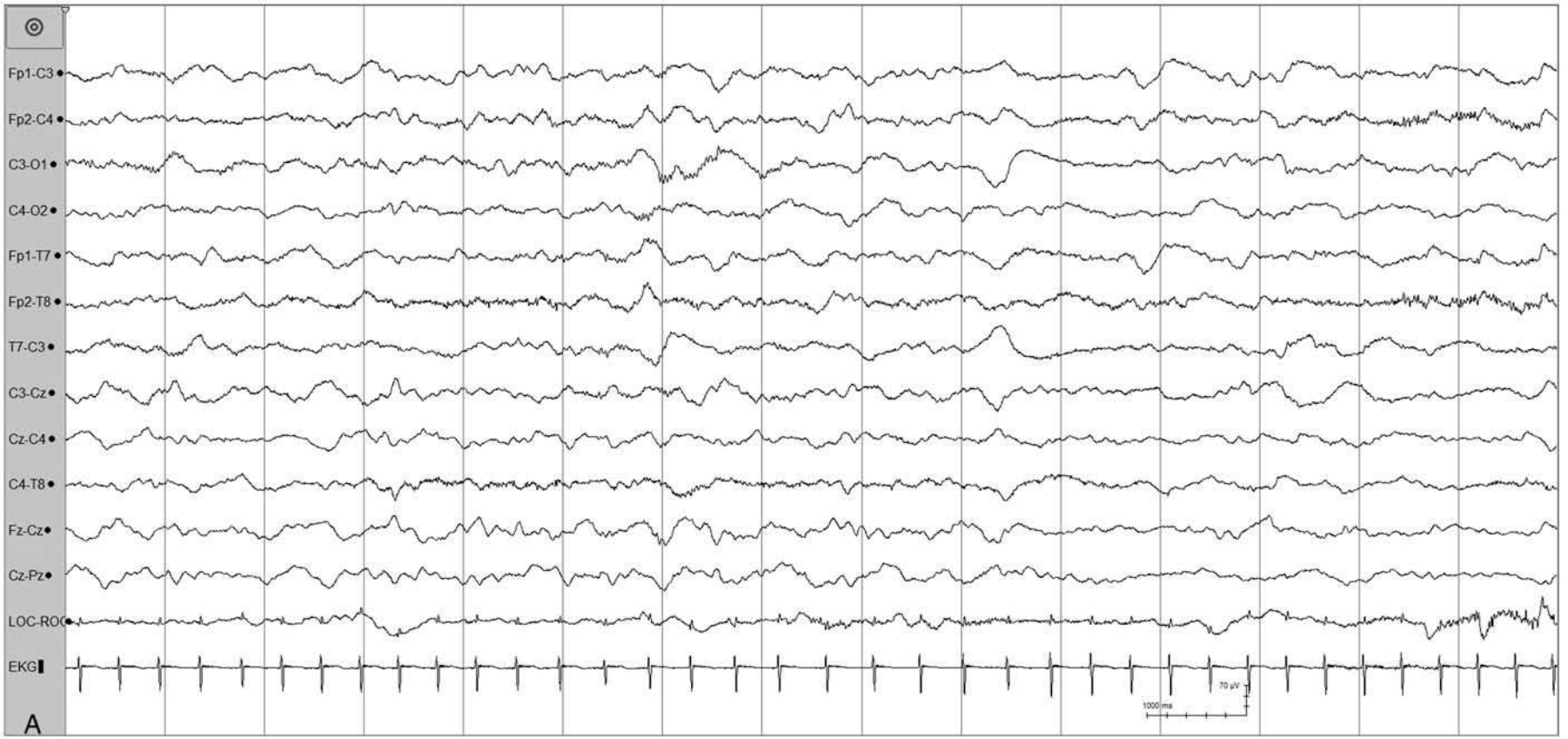

Figure 4.34 (A) and (B) 38 to 40 weeks CA. *Tracé alternant* with repetitive periods of attenuation. (A) Awake: continuous, synchronous, polyfrequency activity in a 40-week CA infant (15 second segment). (*continued*)

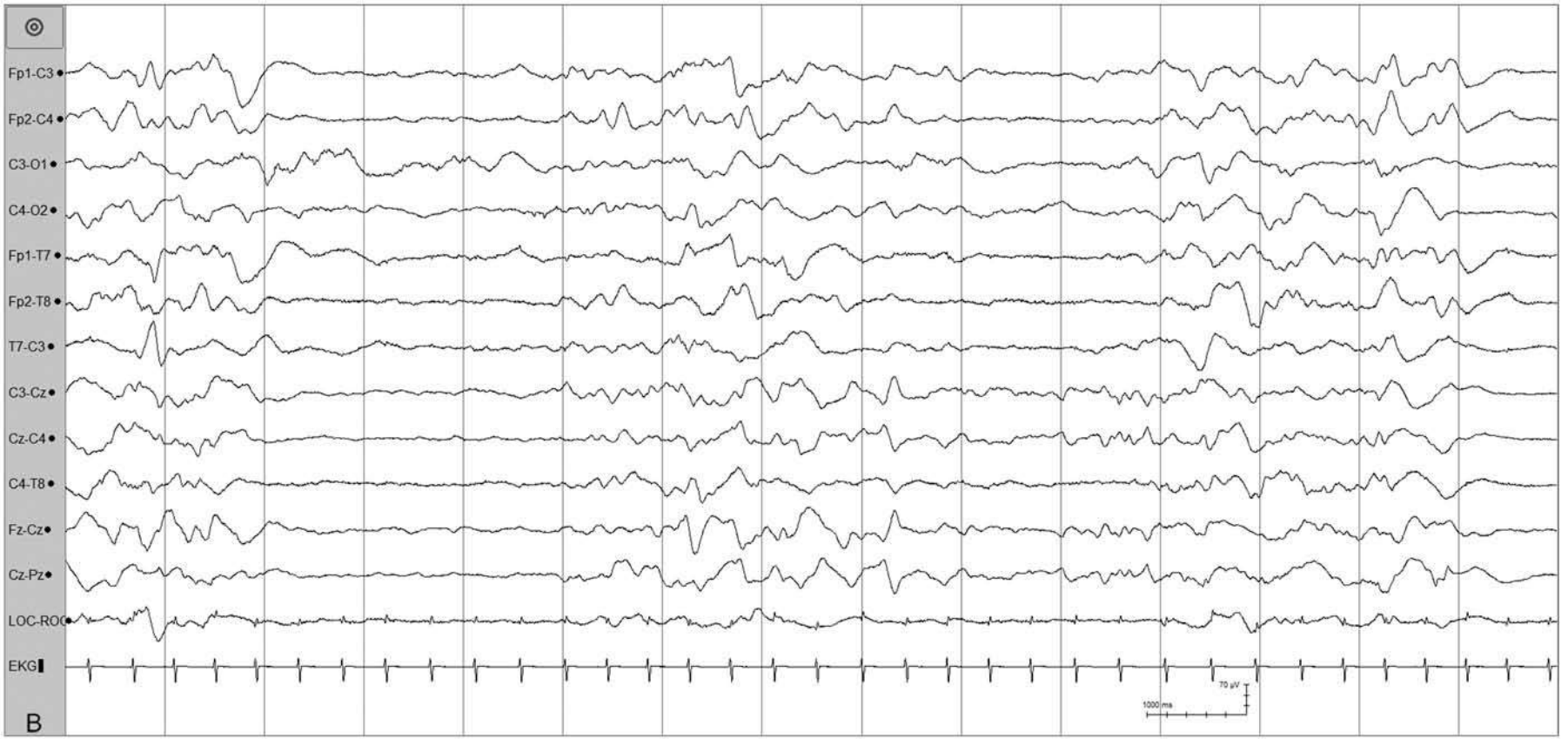

Figure 4.34 (*continued*) **(B)** NREM sleep: *Tracé alterant* sleep in the same recording of this infant (15 second segment).

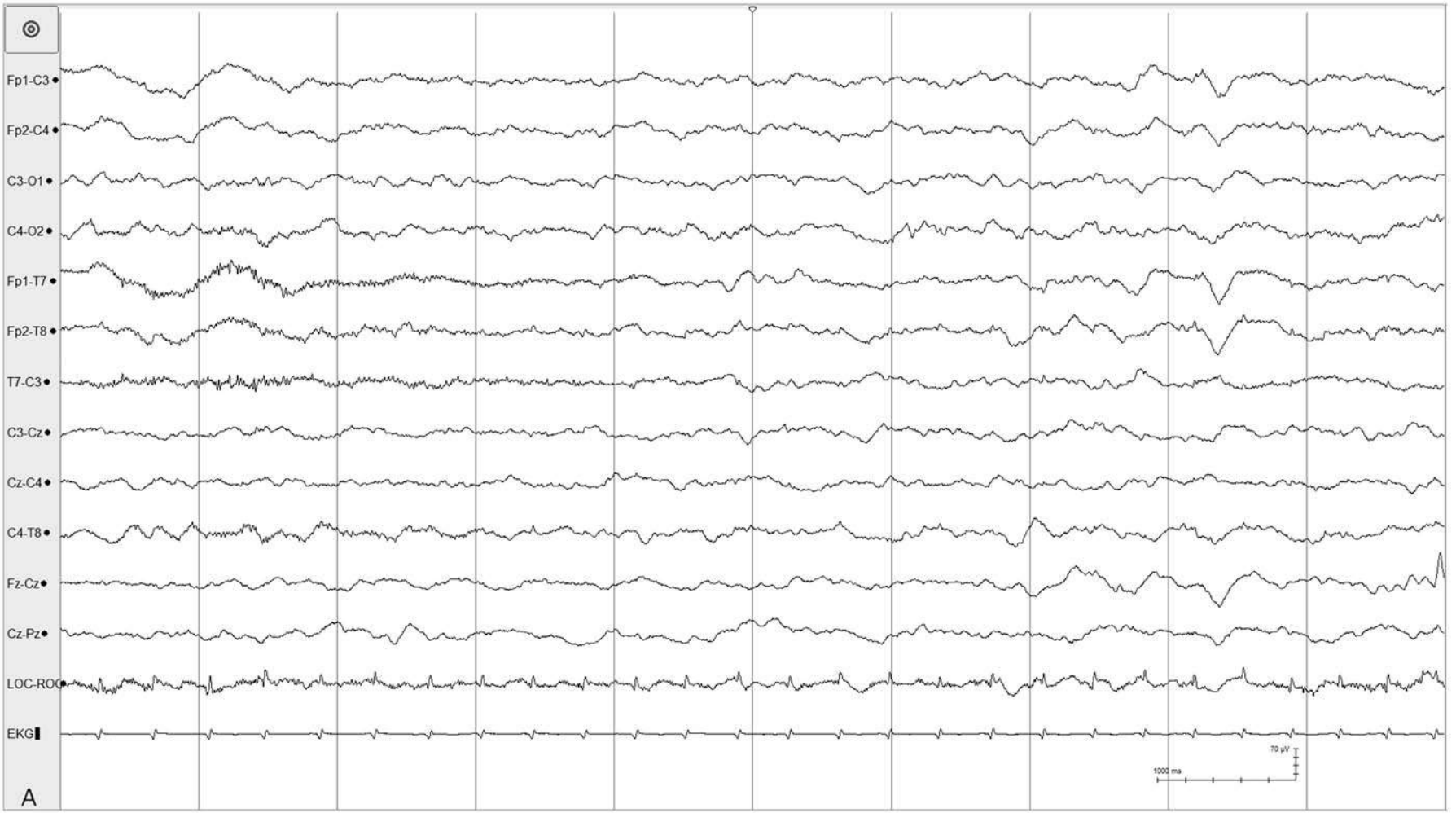

Figure 4.35 (A) and (B) 38 to 40 weeks CA. *Tracé alternant* with a brief period of attenuation. (A) Awake: continuous, synchronous, polyfrequency activity with frontal sharp tranients in a 40-week-CA infant. (*continued*)

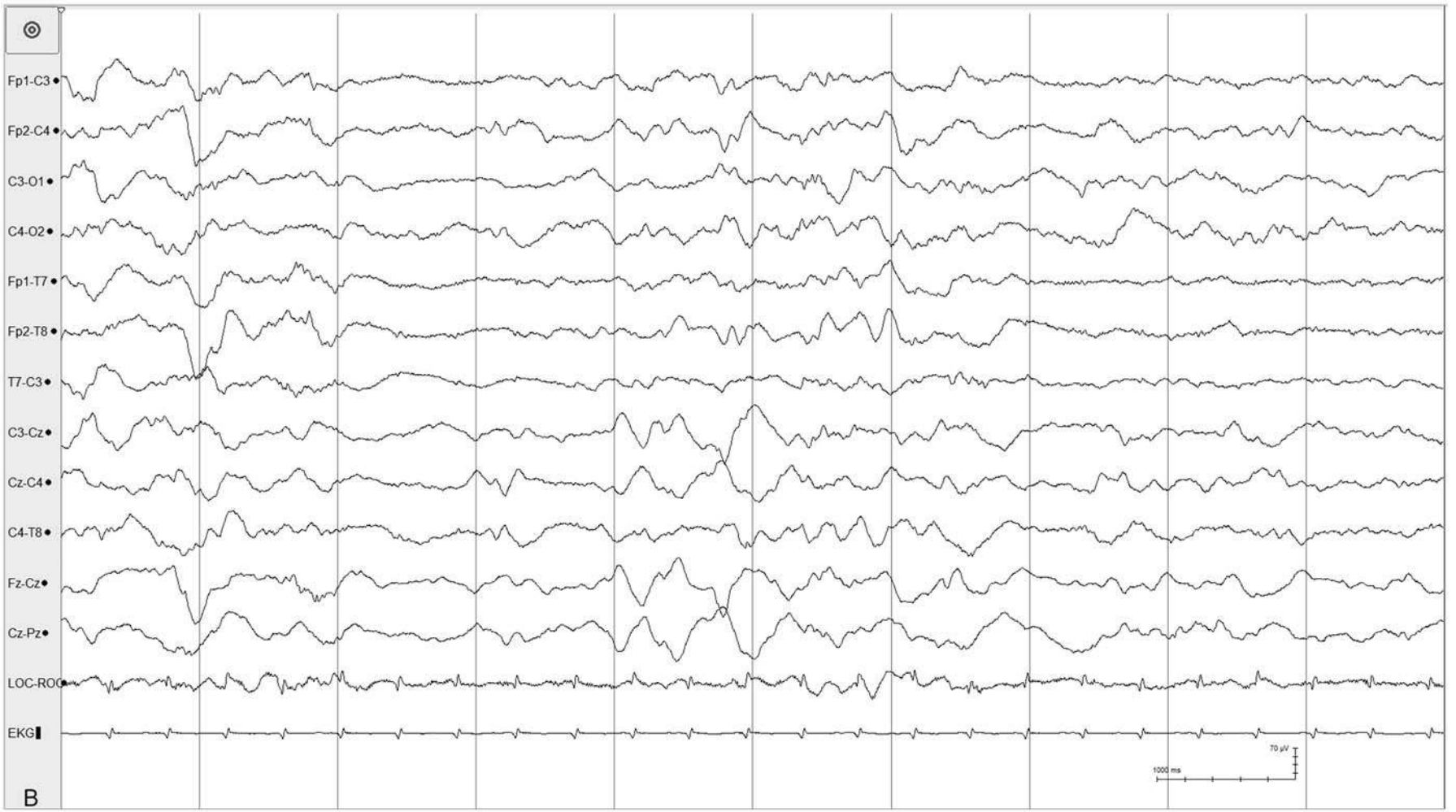

Figure 4.35 (*continued*) **(B)** NREM sleep: *Tracé alterant* in the same recording of this infant with relatively brief period of attenuation.

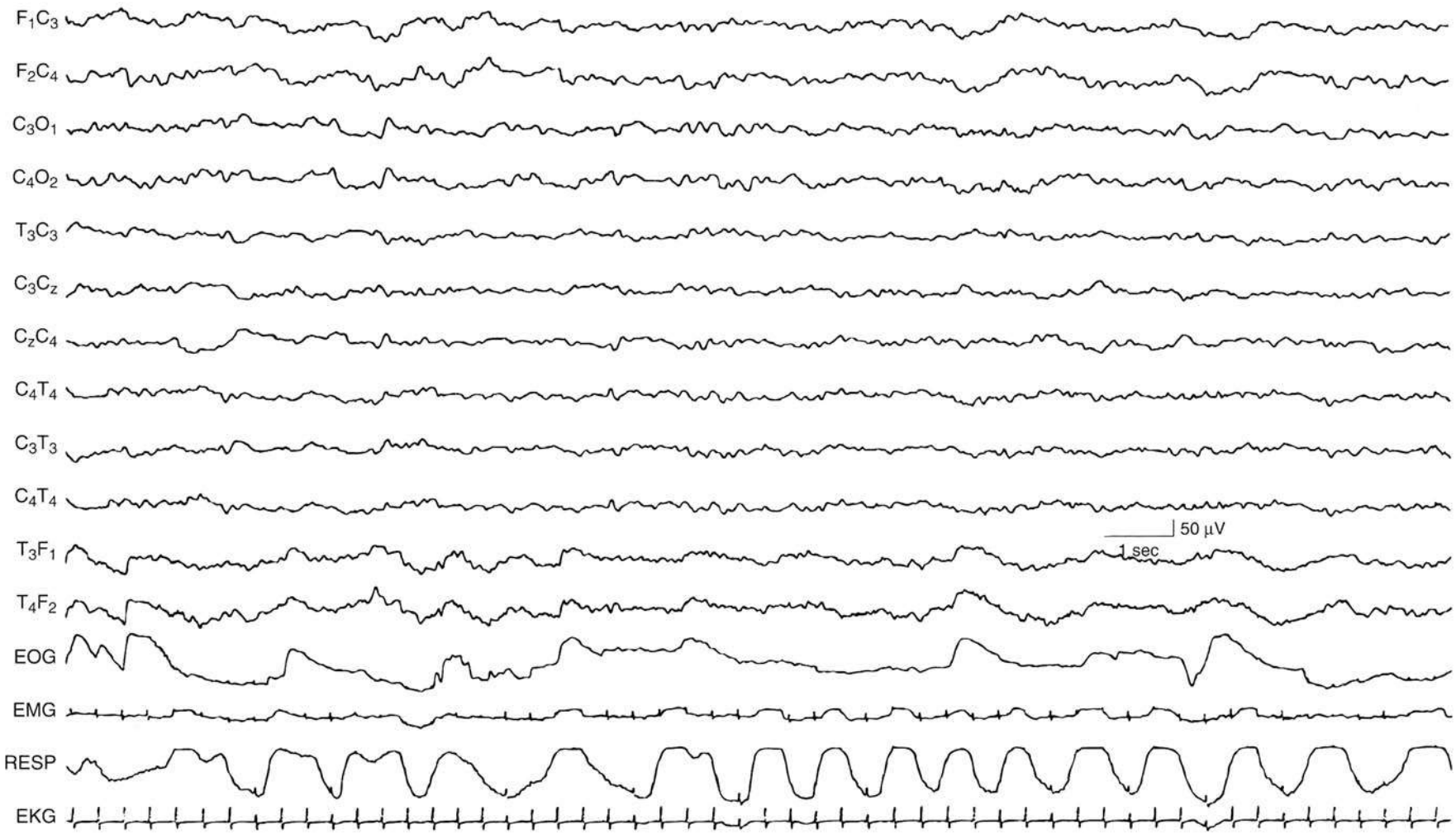

Figure 4.36 38 to 40 weeks CA. REM (active) sleep. There is continuous, synchronous EEG activity. Respiration is irregular and there are REMs (recorded on the EOG channel). (Hrachovy, 2000, with permission.)

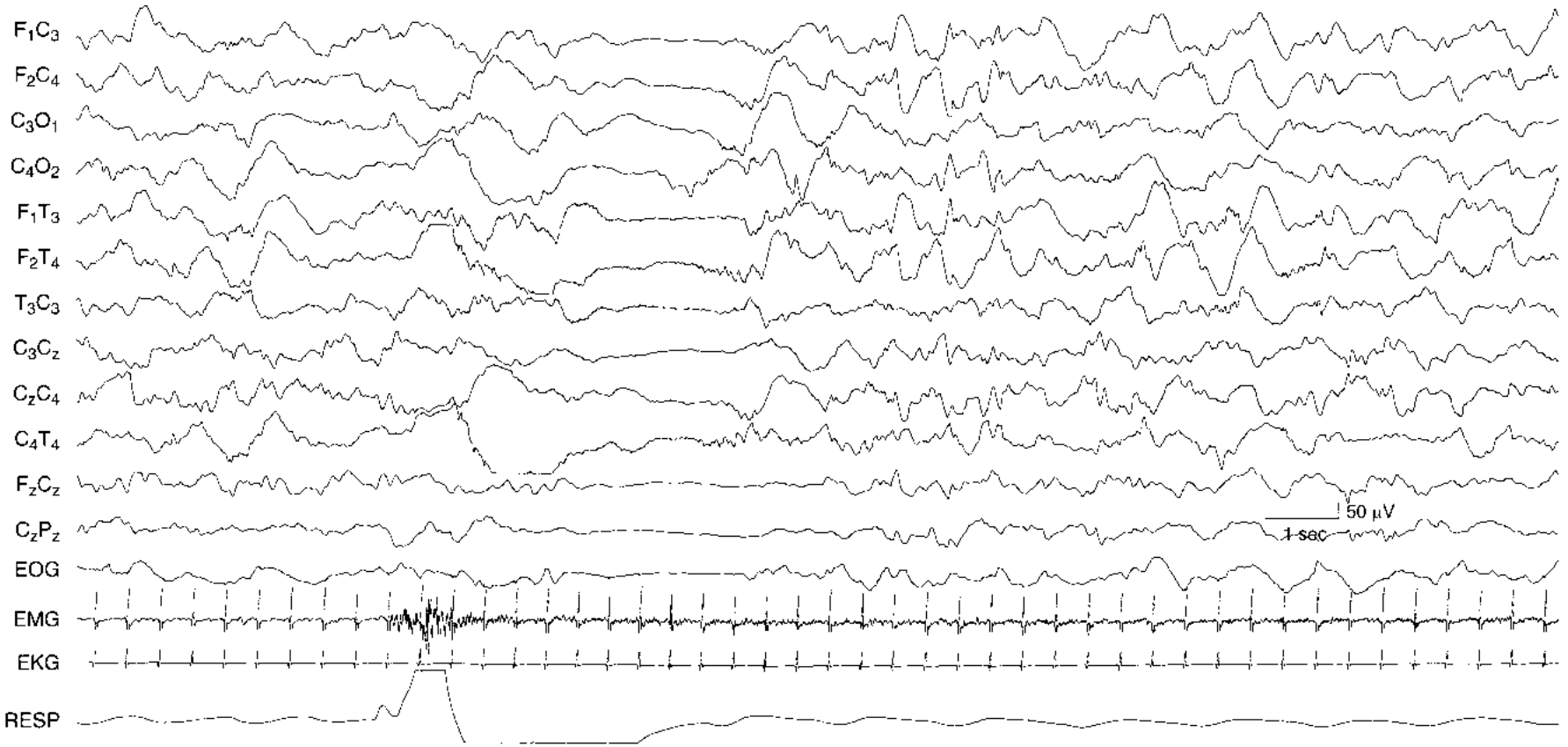

Figure 4.37 38 to 40 weeks CA. Transient arousal: generalized voltage attenuation. The background activity is consistent with NREM (quiet) sleep. There is a brief episode of generalized voltage attenuation associated with clinical arousal (the EMG and respiration channels indicate movement). After about 2 seconds, the EEG returns to NREM background.

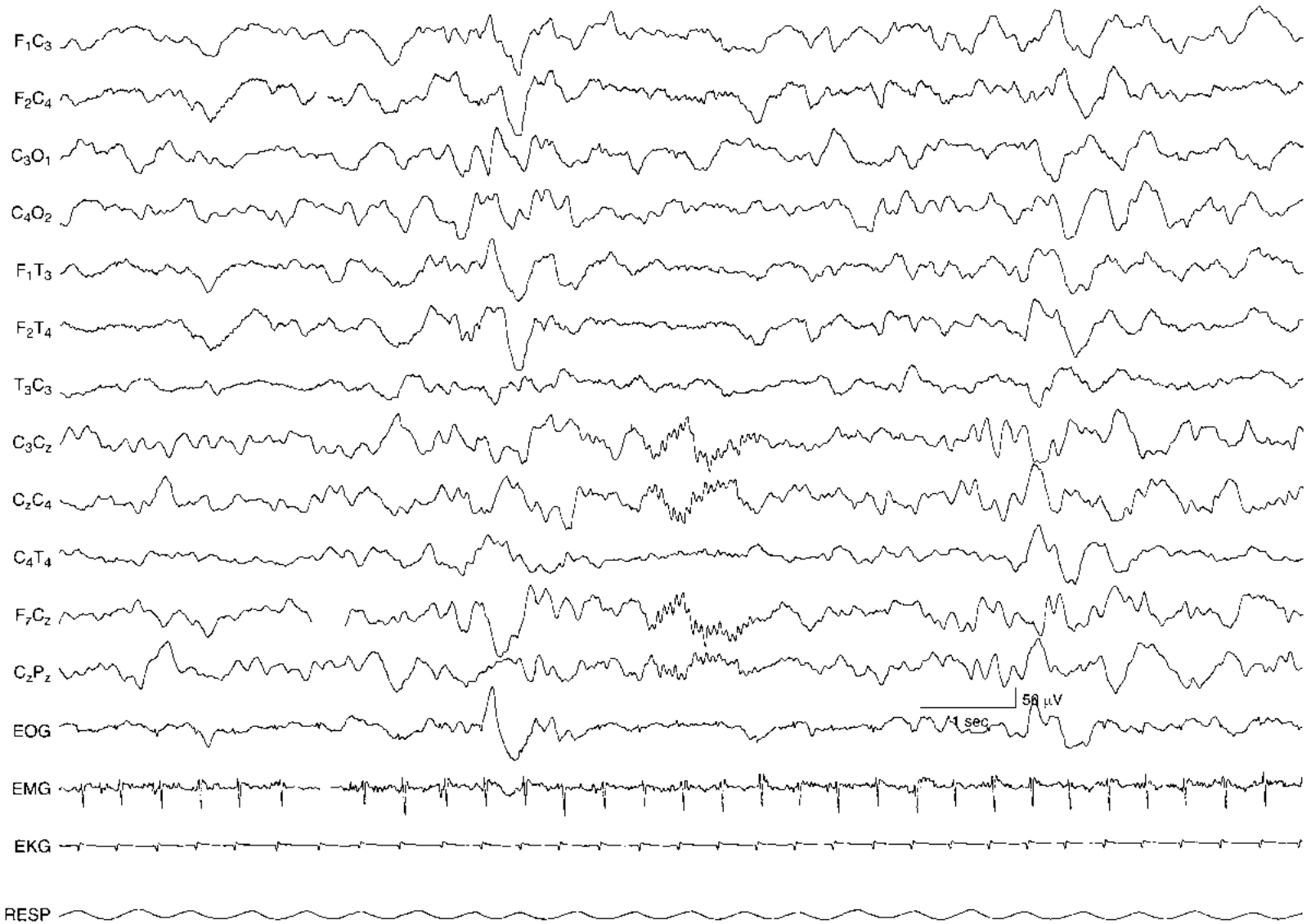

Figure 4.38 41 to 44 weeks CA. Rudimentary sleep spindles. Rudimentary sleep spindles are present in the midline central region in this 43-week CA infant during NREM (quiet) sleep. The background activity is continuous. This is not a typical finding in this CA epoch since spindles are most consistently present after 6 weeks post-term. However, on rare occasions rudimentary spindles do occur earlier and when they first appear are present in the midline central region as shown.

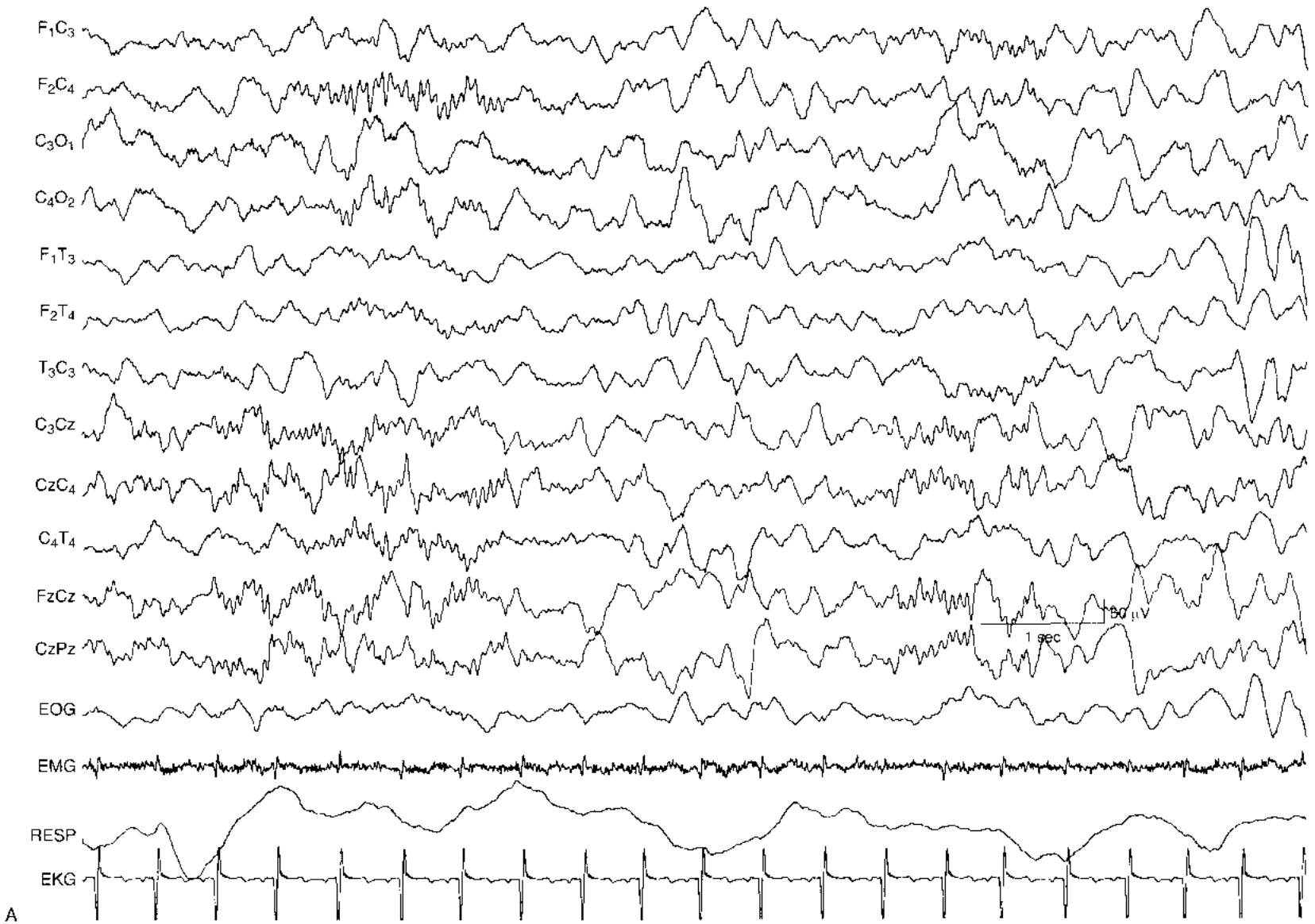

Figure 4.39 (A) and (B) 45 to 48 weeks CA. Sleep spindles. **(A)** Brief sleep spindles are present first in the right central and then in the left central regions in the EEG of this 46-week CA infant. Both bursts have some midline central localization. (*continued*)

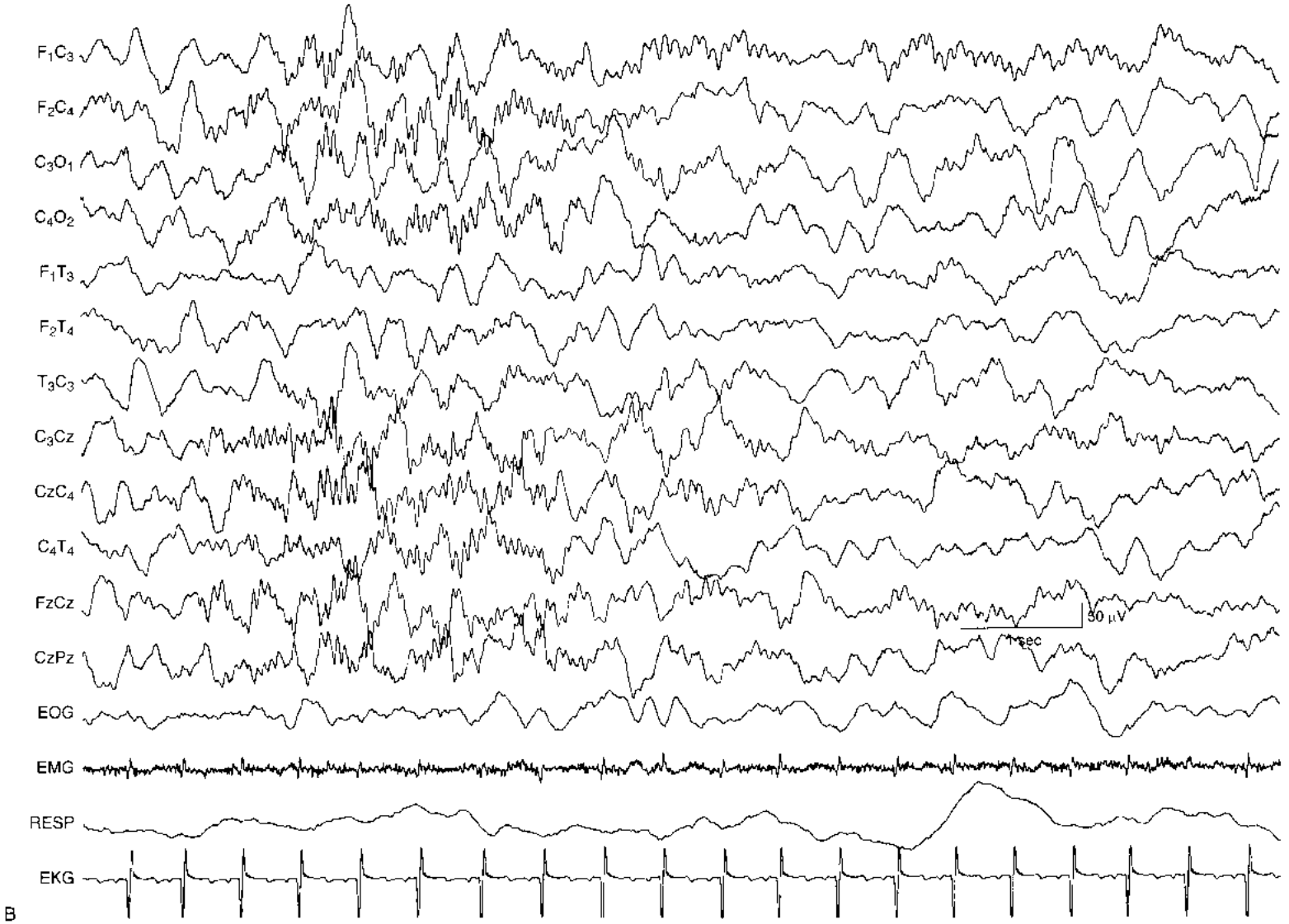

Figure 4.39 (*continued*) **(B)** This sample is a continuation of the previous sample **(A)**. Now the spindles are longer with the one on the right beginning first, overlapping in time with that on the left. The spindles on the two sides occur simultaneous for a few seconds then the spindle on the right subsides while that on the left persists for several seconds.

CHAPTER 5

Patterns of Uncertain Diagnostic Significance

A number of waveforms and patterns have not been reported to occur in normal infants, do not fit the criteria of normality, and are not associated with well-defined abnormal clinical correlates. These patterns are of questionable or uncertain diagnostic significance.

FOCAL SHARP WAVES

Currently, little understanding exists of the significance of focal sharp waves in premature and term infants. Various definitions of "normal" spikes and sharp waves have been proposed. For example, sharp waves occurring two or three times in an hour-long recording may have no significance in the newborn. To be considered normal, sharp waves occurring more frequently than this must be truly random and without persistent focality (Monod et al., 1972) and may arise from any scalp location (Engel, 1975; Hagne, 1972; Schulte, 1970). However, no stringent criteria have been developed to separate, unambiguously, abnormal from normal sharp-wave activity in the newborn.

Sharp waves or sharp-and-slow-wave complexes are commonly recorded from the midtemporal region during sleep in apparently normal premature and term infants. The features our group uses to differentiate between normal and abnormal temporal sharp waves are as follows:

Amplitude and Duration

In general, as the amplitude and duration of sharp waves increase, so does the likelihood that they are abnormal. For example, in a premature or term infant, random midtemporal sharp waves having a voltage of less than 75 μV, a duration of less than 100 msec, and occurring only rarely during sleep, would be considered normal (**Figure 5.1**). Conversely, midtemporal sharp waves with a voltage exceeding 150 μV and a duration greater than 150 msec would be considered abnormal. Unfortunately, numerous temporal sharp waves fall in a "gray zone" by these criteria. The most controversial is that of amplitude, since some sharp waves of greater than 100 μV may be considered normal if they are normal by all other parameters. However, other features, discussed in this section, often aid the neurophysiologist in determining the probability of normality or abnormality.

Incidence and Persistence

Temporal sharp waves that are considered normal occur randomly. They usually occur bilaterally but asynchronously and may be symmetrical or asymmetrical (**Figure 5.2**). Generally, these sharp waves appear infrequently; thus, temporal sharp waves occurring in quick succession, in series or long runs, and occurring on only one side are likely to be considered abnormal (**Figures 5.3–5.5**).

Morphology and Complexity of Waveforms

Temporal sharp waves classified as normal are usually mono- or diphasic. The morphology of abnormal temporal sharp waves is more variable. Although they are sometimes mono- or diphasic, abnormal sharp waves more often are polyphasic and followed by a high voltage slow wave (**Figures 5.6–5.9**).

Polarity

The initial component of a normal temporal sharp wave is surface negative. Temporal sharp waves with an initial or prominent surface-positive component are abnormal **(Figure 5.9)**.

Features Associated With Changes in Wake/Sleep States

In the premature infant, normal temporal sharp waves may occur in any state. In the term infant, however, normal temporal sharp waves are more common during transitional sleep. If temporal sharp waves appear in the waking record of term infants, they probably are abnormal, regardless of other characteristics (**Figure 5.10**).

Midtemporal sharp waves satisfying the above criteria of normality occur in some healthy-term newborns during sleep. These sharp waves disappear rapidly during the first month of life and are seen in less than 5% of healthy newborns after 6 weeks post-term. Even temporal sharp waves considered clearly abnormal often do not persist beyond this age.

FOCAL RHYTHMIC ACTIVITY

Midline Frontal Rhythmic Activity

Bursts of rhythmic 50 to 200 μV, 5 to 9 Hz activity may occur in the midline frontal regions of neurologically normal infants between 38 and 42 weeks conceptional age (CA) (Hayakawa et al., 1987). The waves may have a sharp appearance and may occur in brief bursts usually lasting less than 1.5 seconds. They may occur in transitional and nonrapid eye movement (NREM) sleep, but typically not in REM sleep. They have been reported to occur in 55% of neurologically normal term infants, only rarely occur in infants with abnormal outcomes (4% of abnormal infants), and are not present in infants with moderate to severely depressed background activity (Hayakawa et al., 1987).

Midline Central Rhythmic Activity

Rhythmic activity similar to the frontal midline activity described earlier may also be present in the midline central in an otherwise normal electroencephalography (EEG) (Hrachovy et al., 1990) (**Figures 5.11–5.13**). This activity may also accompany other EEG features that are considered abnormal, particularly central sharp waves, in infants who have experienced various central nervous system (CNS) insults.

Occipital Rhythmic Theta Activity

In the term infant's EEG, an uncommon finding is the occurrence of brief runs of rhythmic 4 to 6 Hz, 50 to 100 μV activity in the occipital regions with a duration of less than 1 second. This activity appears in wakefulness or sleep and usually occurs asynchronously on the two sides (**Figure 5.14**). In some infants, this activity may be unilateral (**Figure 5.15**). Occipital rhythmic theta activity can occur as an isolated feature in an otherwise normal EEG, but usually it accompanies other abnormalities such as sharp waves or an abnormal background.

TRANSIENT UNILATERAL ATTENUATION OF BACKGROUND ACTIVITY DURING SLEEP

Transient unilateral attenuation of background EEG activity occurring during NREM sleep is an unusual finding reported to occur in about 3% to 4% of all newborns (Challamel et al., 1984; O'Brien et al., 1987) (**Figures 5.16 and 5.17**). The attenuation episodes usually last about 1 minute and begin and end abruptly. The background EEG activity is normal in many infants. In our experience, these episodes usually occur only once during a recording session and usually within minutes of the time the infant first enters NREM sleep.

The significance of this finding, which occurs in apparently normal as well as in abnormal infants, has not been determined. Such episodes of unilateral attenuation of background activity should not be confused with the more common finding of marked generalized and/or lateralized voltage attenuation seen in the EEGs of infants who have experienced a variety of CNS insults. The latter attenuation episodes are short in duration (2–15 sec), occur repeatedly during the recording session, and may be present in all wake/sleep states. The isolated transient unilateral attenuation episodes seen in NREM sleep, and the generalized and/or lateralized attenuation episodes associated with various CNS insults, must also be distinguished from the generalized attenuation of background EEG activity that is seen when transient arousal occurs from NREM sleep.

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Transient Unilateral Attenuation of Background Activity During Sleep

Figure 5.16 Transient unilateral attenuation of background activity during sleep.
Figure 5.17 Transient unilateral voltage attenuation.

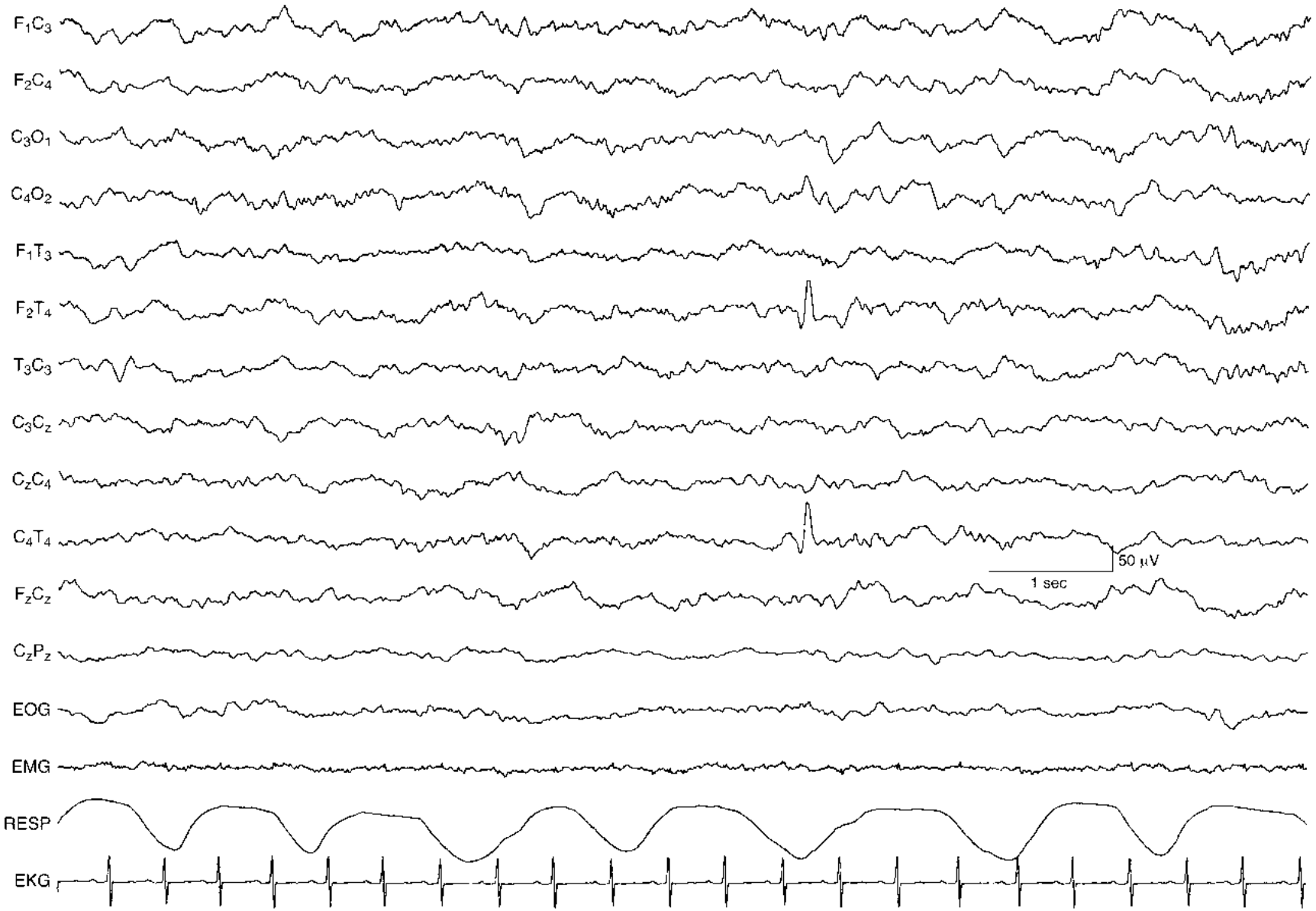

Figure 5.1 Randomly occurring right temporal sharp wave. An isolated diphasic sharp wave is present in the right temporal region with features that suggest it is a normal phenomenon. The background EEG of this sleeping 40-week CA infant is normal.

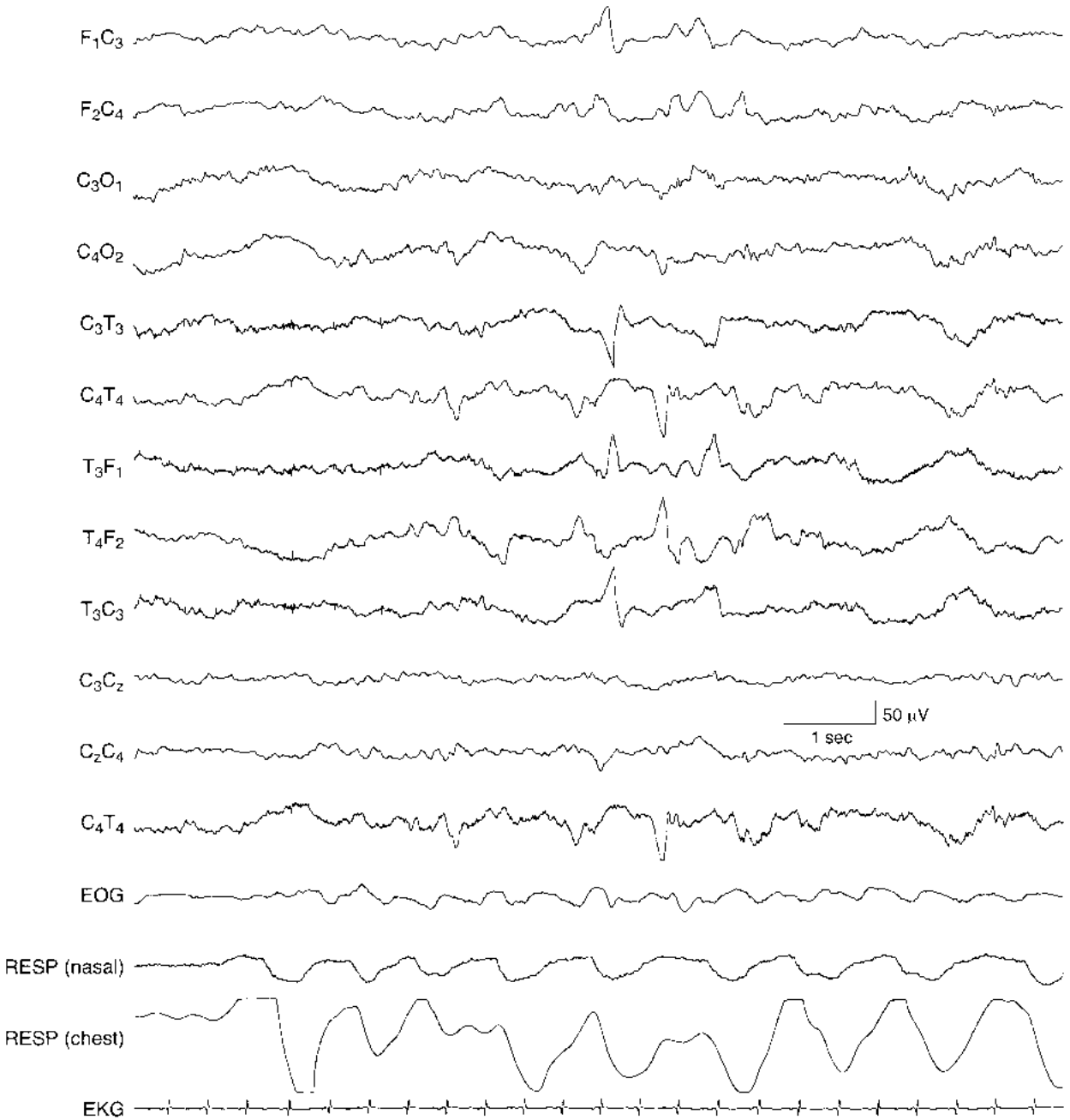

Figure 5.2 Independent, symmetrical, bilateral temporal sharp waves. Sharp waves are present in the left and right temporal regions appearing asynchronously, but symmetrically. The bilateral and asynchronous nature of the sharp waves is a normal finding. However, their amplitudes are near or greater than 150 µV and their durations are relatively long suggesting abnormality. The background activity is normal in this 40-week CA infant.

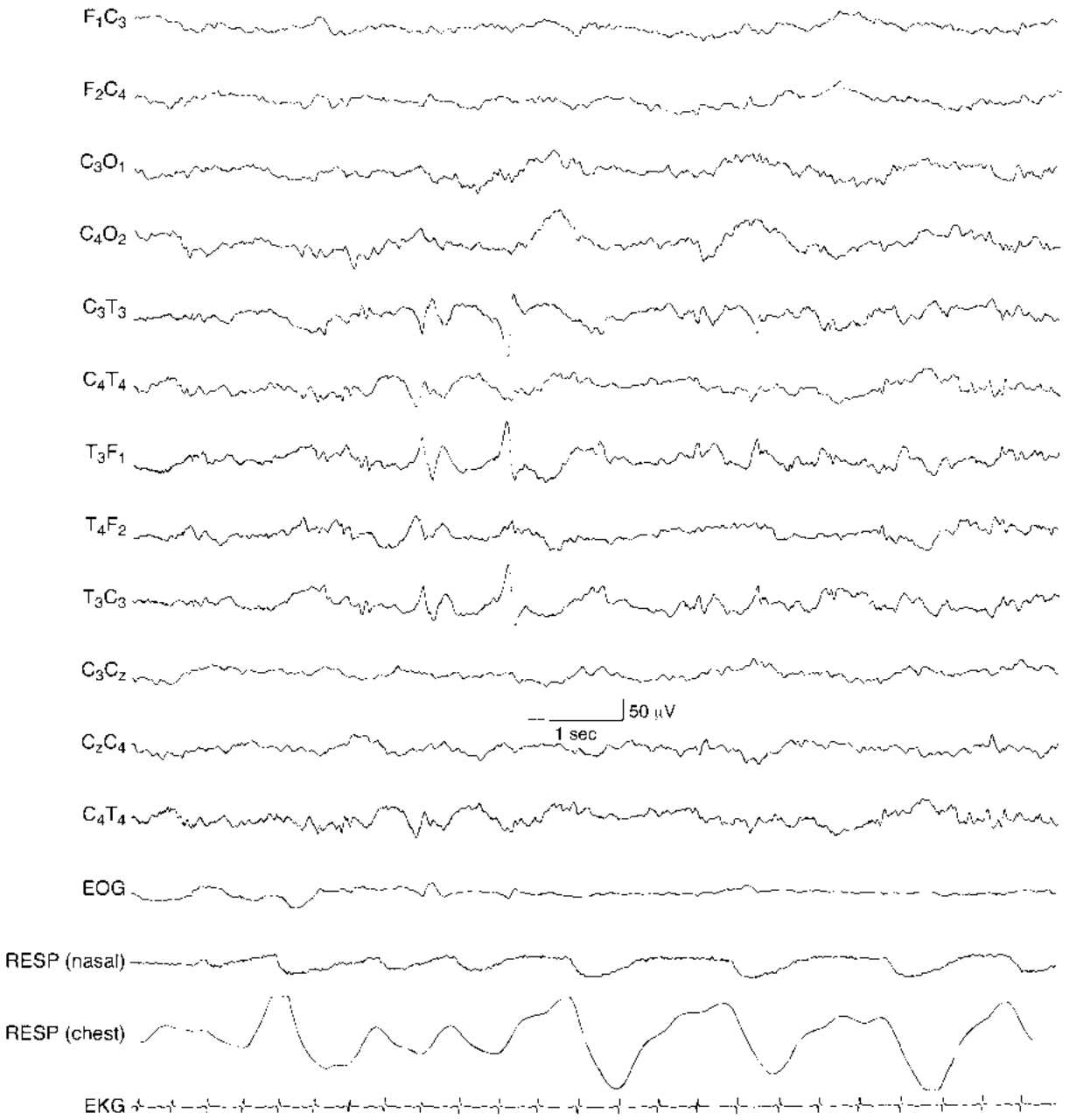

Figure 5.3 Repetitive left temporal sharp waves. Recurring sharp waves are present in the left temporal region in this 40-week CA infant with normal EEG background activity. Only two sharp waves are present in this sample. Thus, although repetitive, the degree of repetition is marginal, suggesting normality.

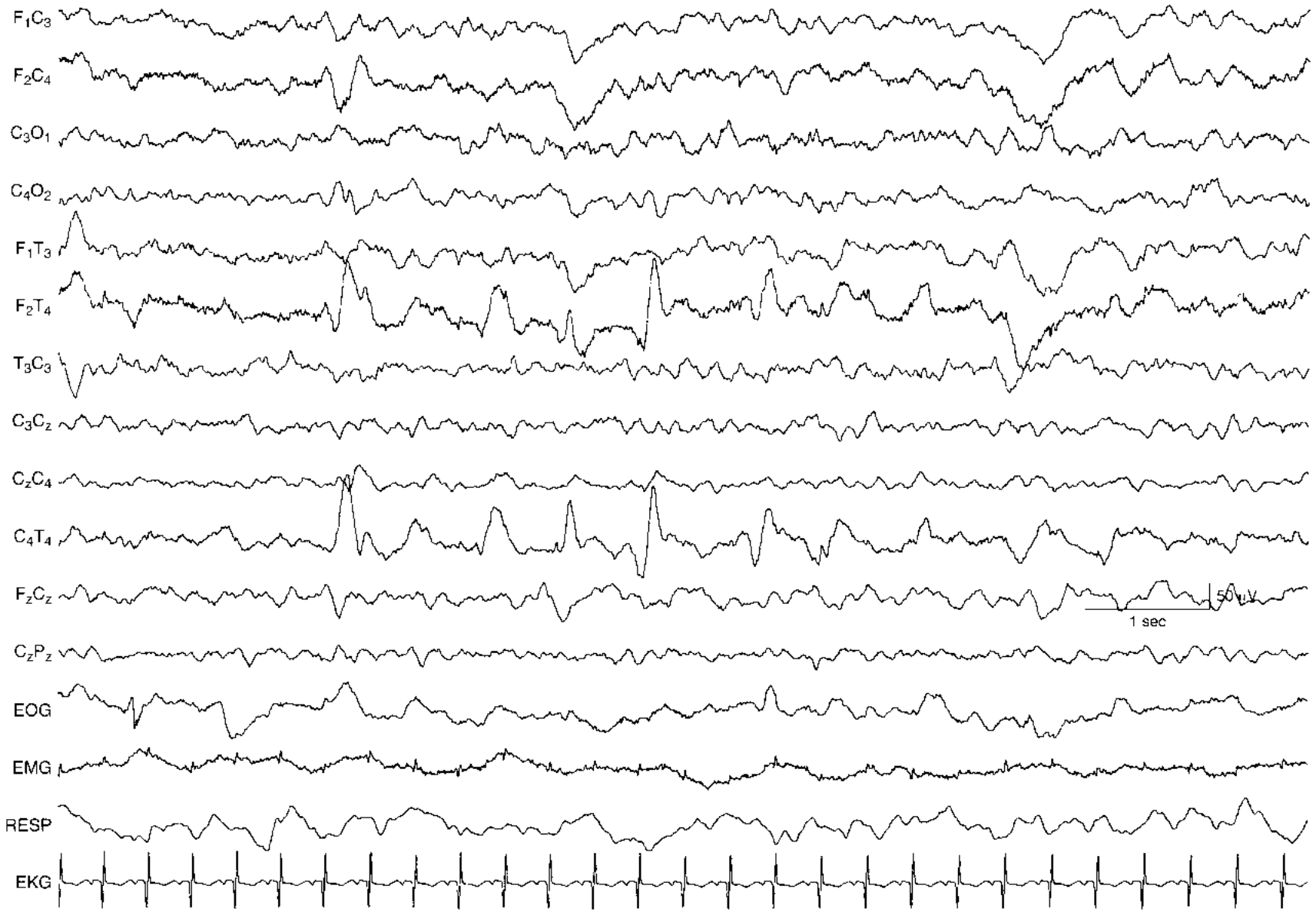

Figure 5.4 Repetitive right temporal sharp waves. The temporal sharp waves on the right are repetitive. They are also high in amplitude. These features suggest abnormality. The background EEG activity is normal in this 40-week CA infant (low frequency filter, 0.16 Hz).

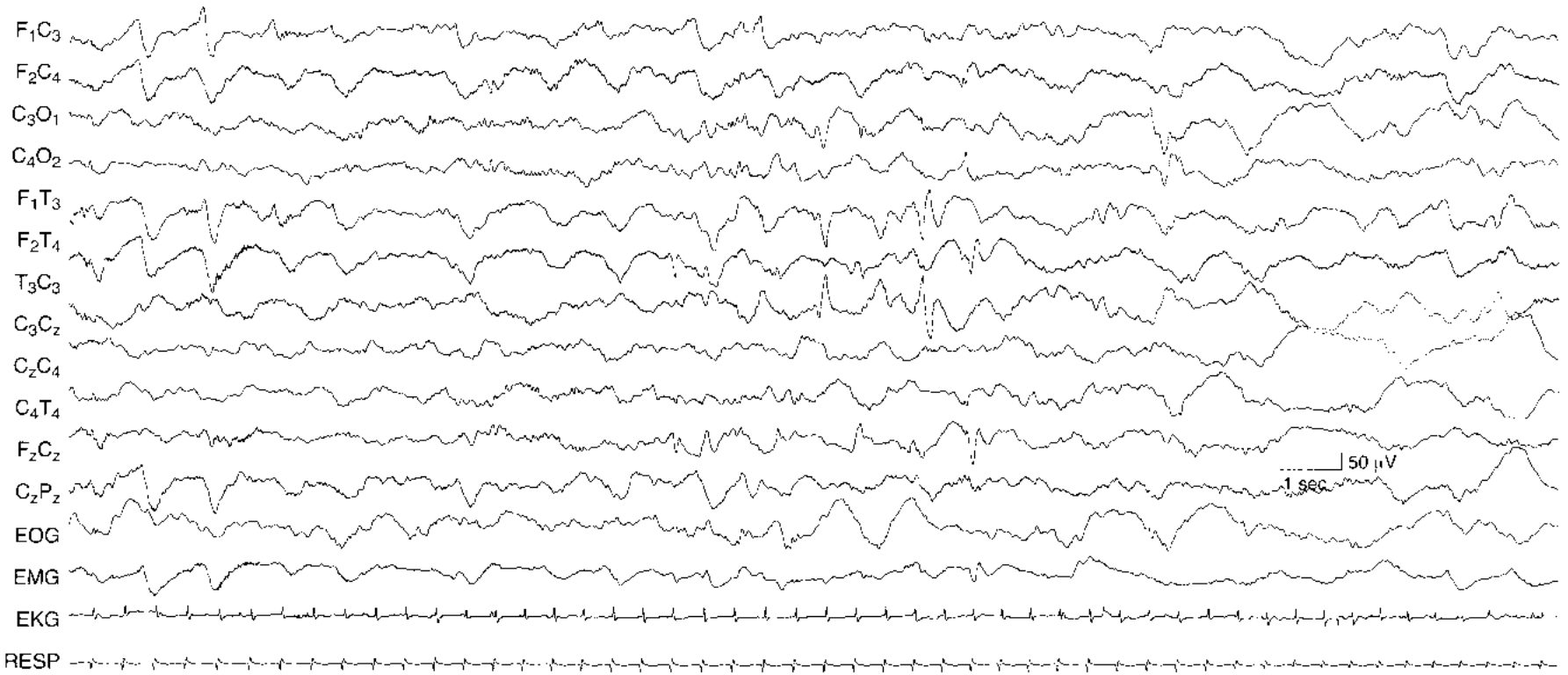

Figure 5.5 Repetitive, independent, bilateral temporal sharp waves. Runs of sharp waves are present in the left and right temporal regions, more prominently on the left where the sharp waves are more frequent and higher in amplitude than those on the right. Their repetitive occurrence and the high amplitude of some of the waves and their association with slow waves on the left suggest abnormality. Note the frontal sharp transients in the early portion of the sample; their occurrence is a normal phenomenon at this CA. This sleeping infant is 40-week CA and there is normal background EEG activity.

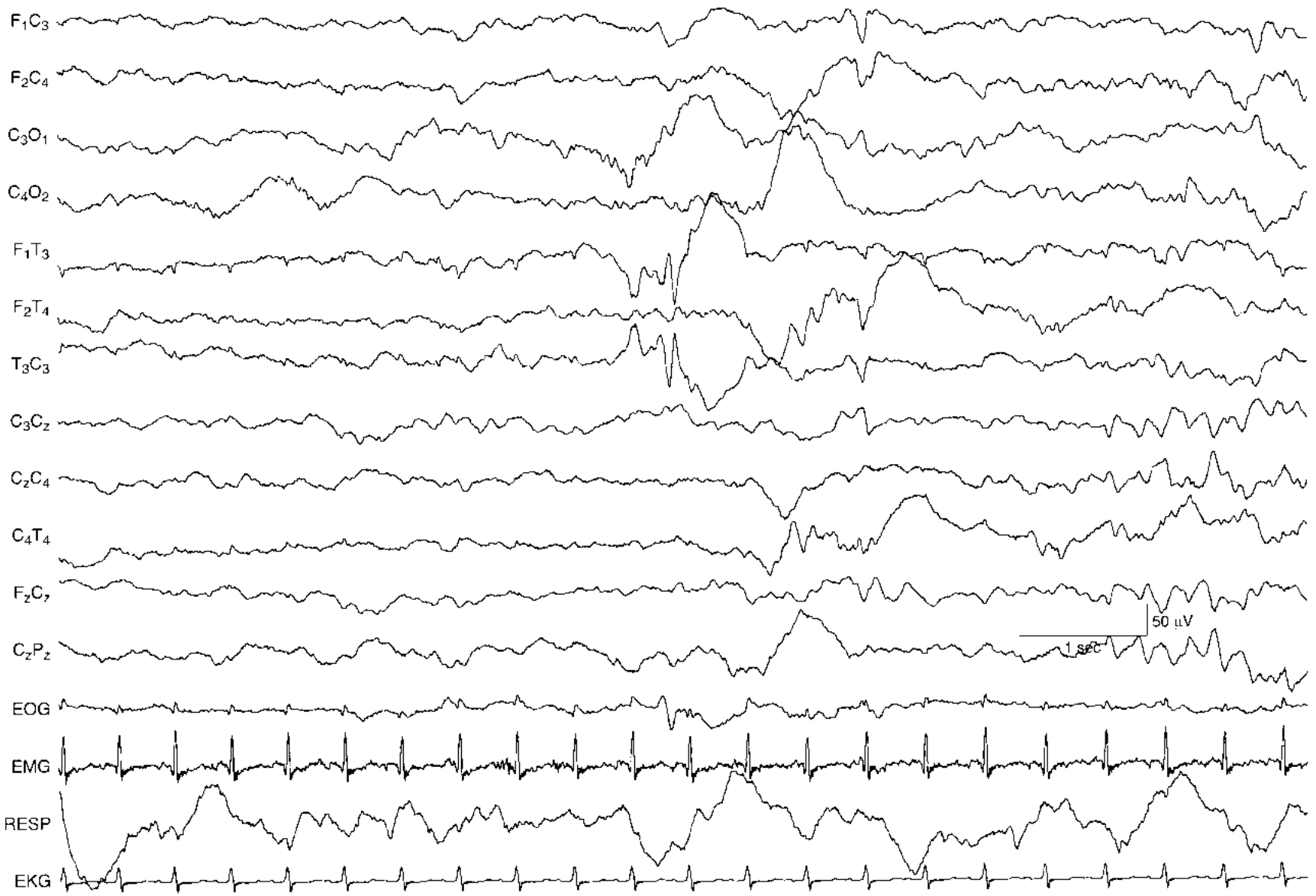

Figure 5.6 Sharp- and slow-wave morphology. A temporal sharp wave is present on the left that is normal in morphology and marginal in amplitude. However, the high-voltage slow wave that follows the sharp wave—creating a sharp- and slow-wave complex—suggests that this is an abnormal finding. This 42-week CA infant is in nonrapid eye movement (NREM) (quiet) sleep. The background activity is normal.

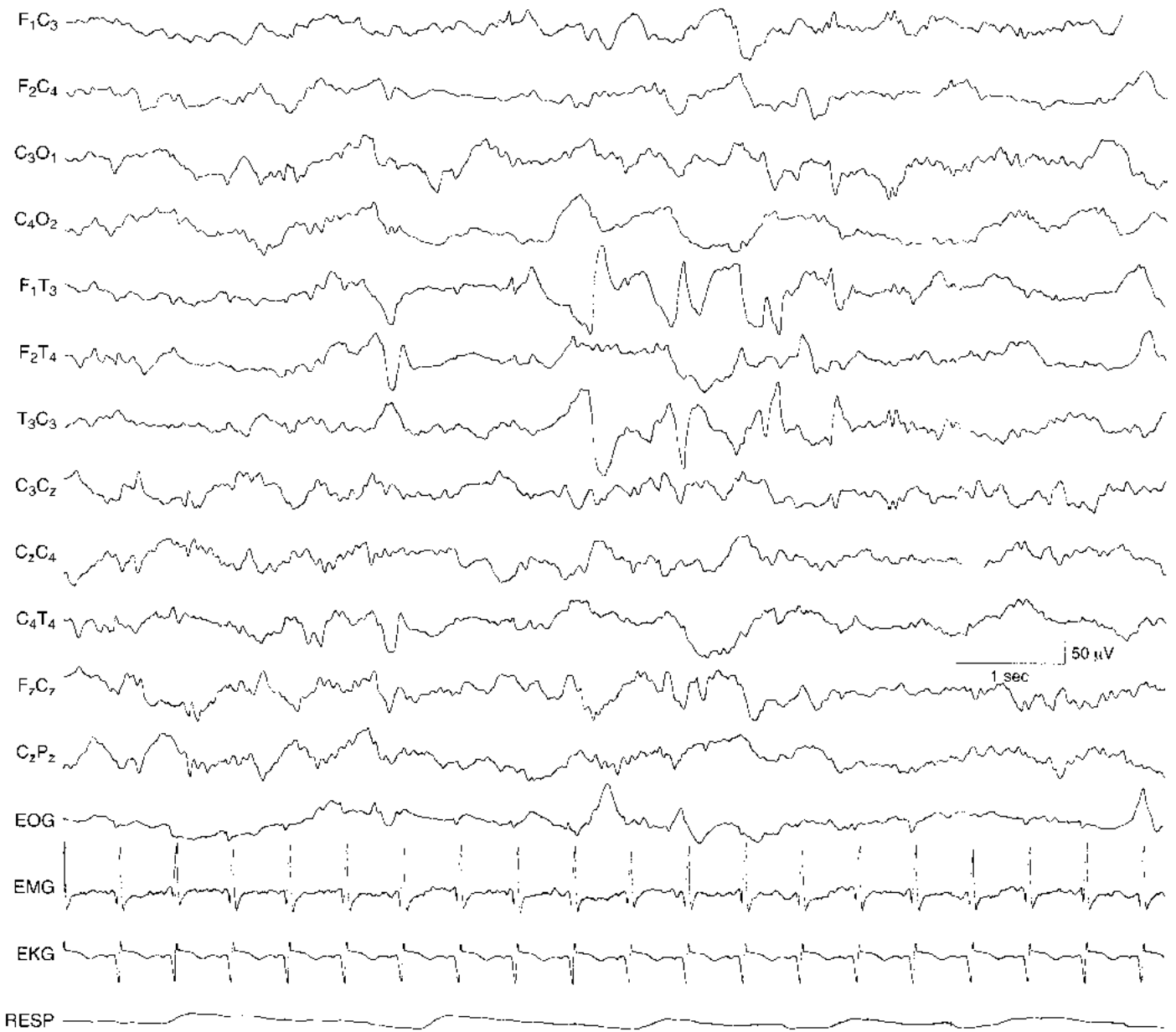

Figure 5.7 Complex morphology of left temporal sharp waves. The morphology of the sharp wave activity in the left temporal region is relatively complex, with slow and fast components and some waveforms that are sharper than others, suggesting abnormality. The background EEG activity is normal in this 38-week CA infant.

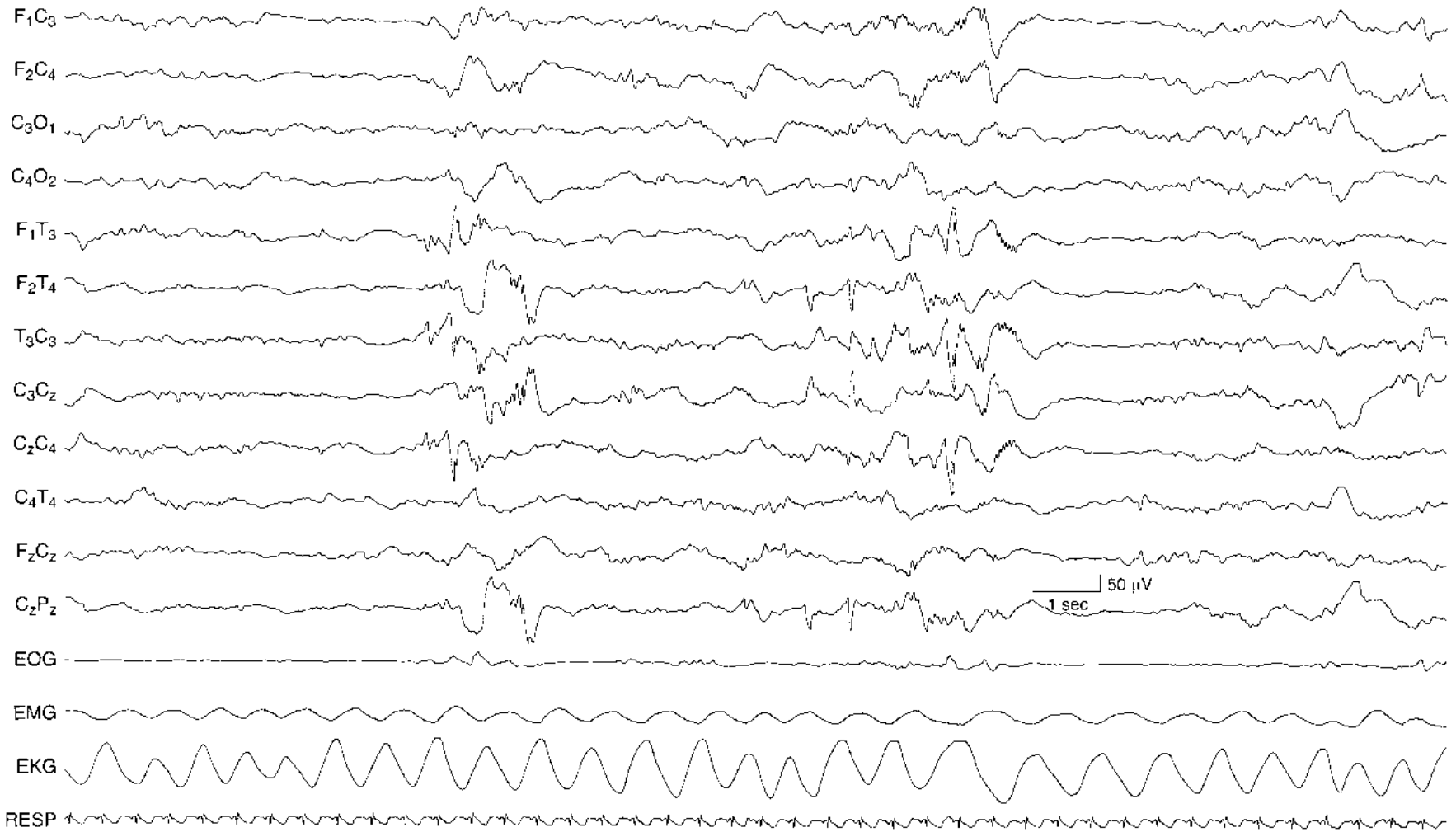

Figure 5.8 Complex and variable morphology in bilateral, independent temporal sharp waves. Repetitive temporal sharp waves appear independently in the left and right temporal regions with complex morphology, including spike-like waveforms. These features suggest that these temporal sharp waves are abnormal. The background EEG activity is abnormal with brief episodes of generalized voltage attenuation in this 40-week CA infant.

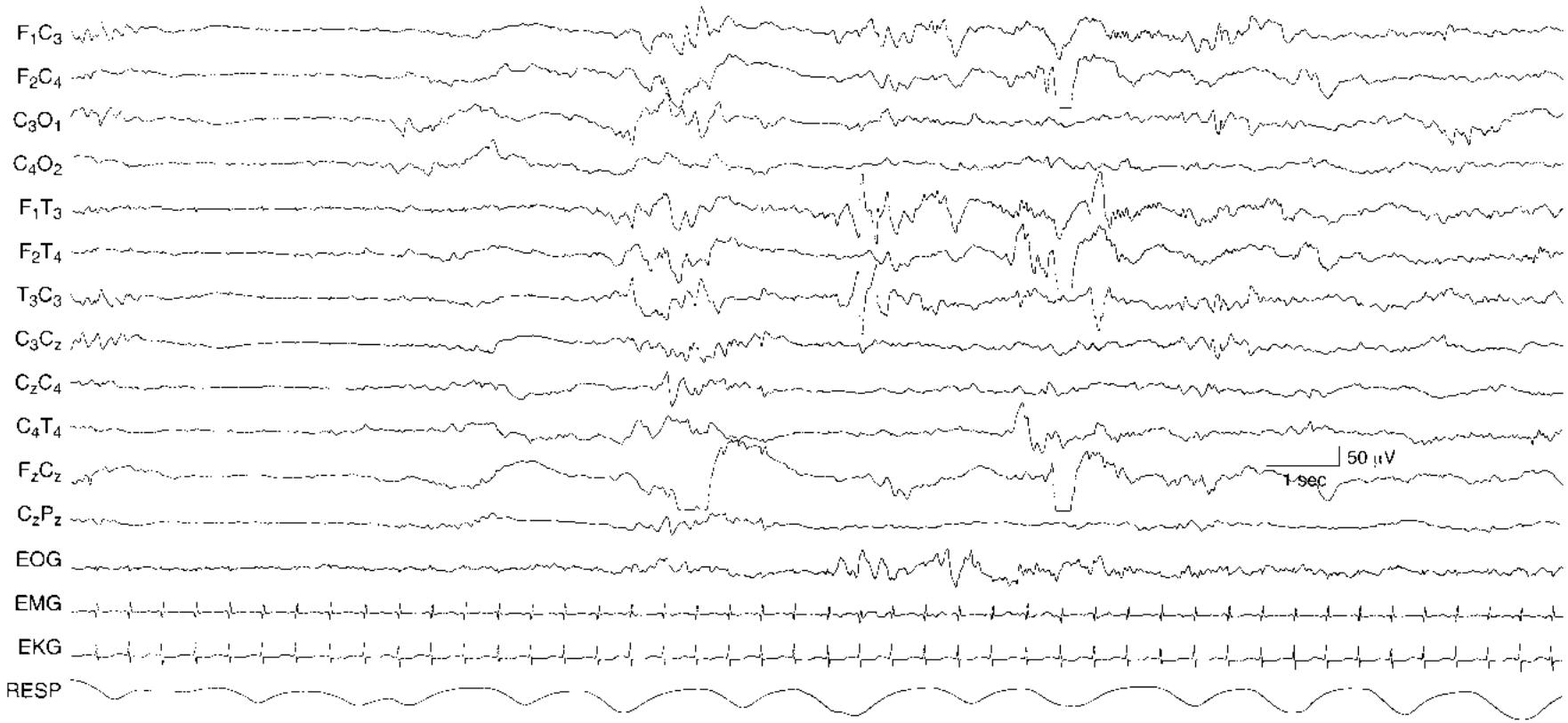

Figure 5.9 Complex morphology and varying polarity of temporal sharp waves. The sharp wave activity appears independently in the left and right temporal regions. There is variable and complex morphology in both regions with waveform components that are both surface negative and surface positive in polarity. The EEG background is abnormal with brief periods of generalized voltage attenuation in this 40-week CA infant.

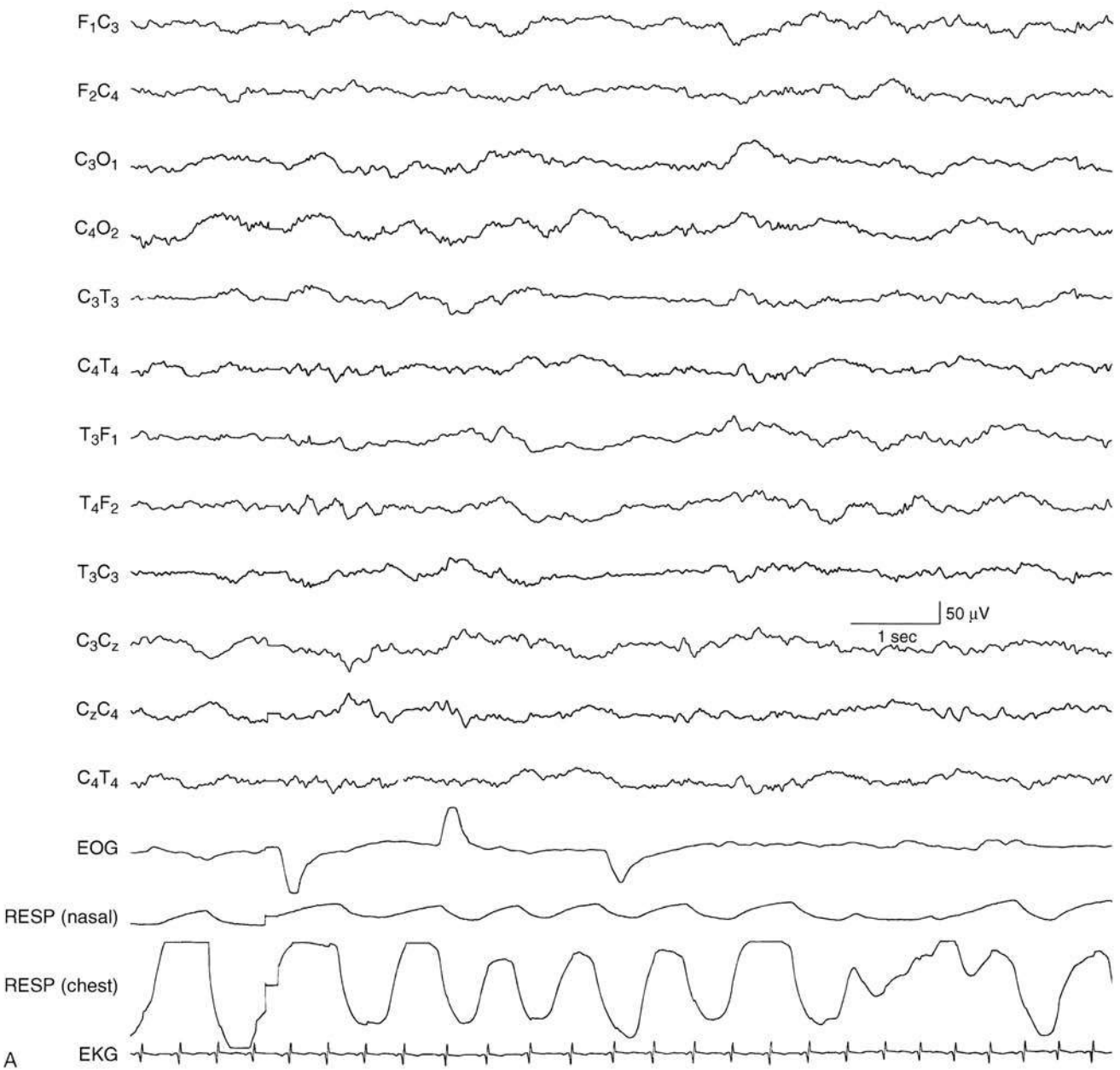

Figure 5.10 (A) and (B) Influence of wake/sleep state on the occurrence of temporal sharp waves: activation of sharp waves during sleep. (A) The awake recording in this 40-week CA infant is normal with continuous polyfrequency activity and no sharp waves. (*continued)*

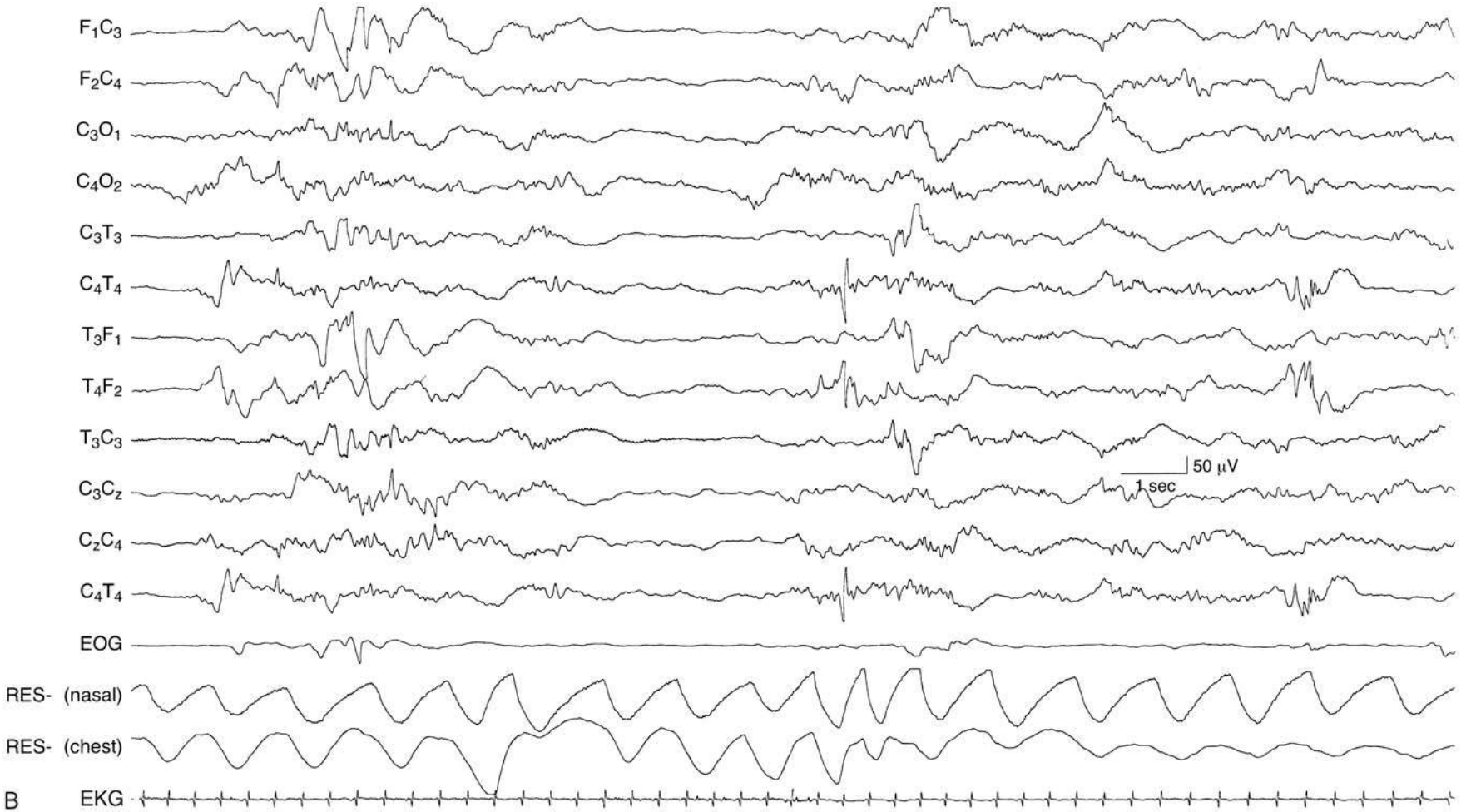

Figure 5.10 (*continued*) **(B)** In NREM (quiet) sleep there are independent, bilateral temporal sharp waves with variable and complex morphology. The background activity is characterized by abnormal periods of generalized voltage attenuation.

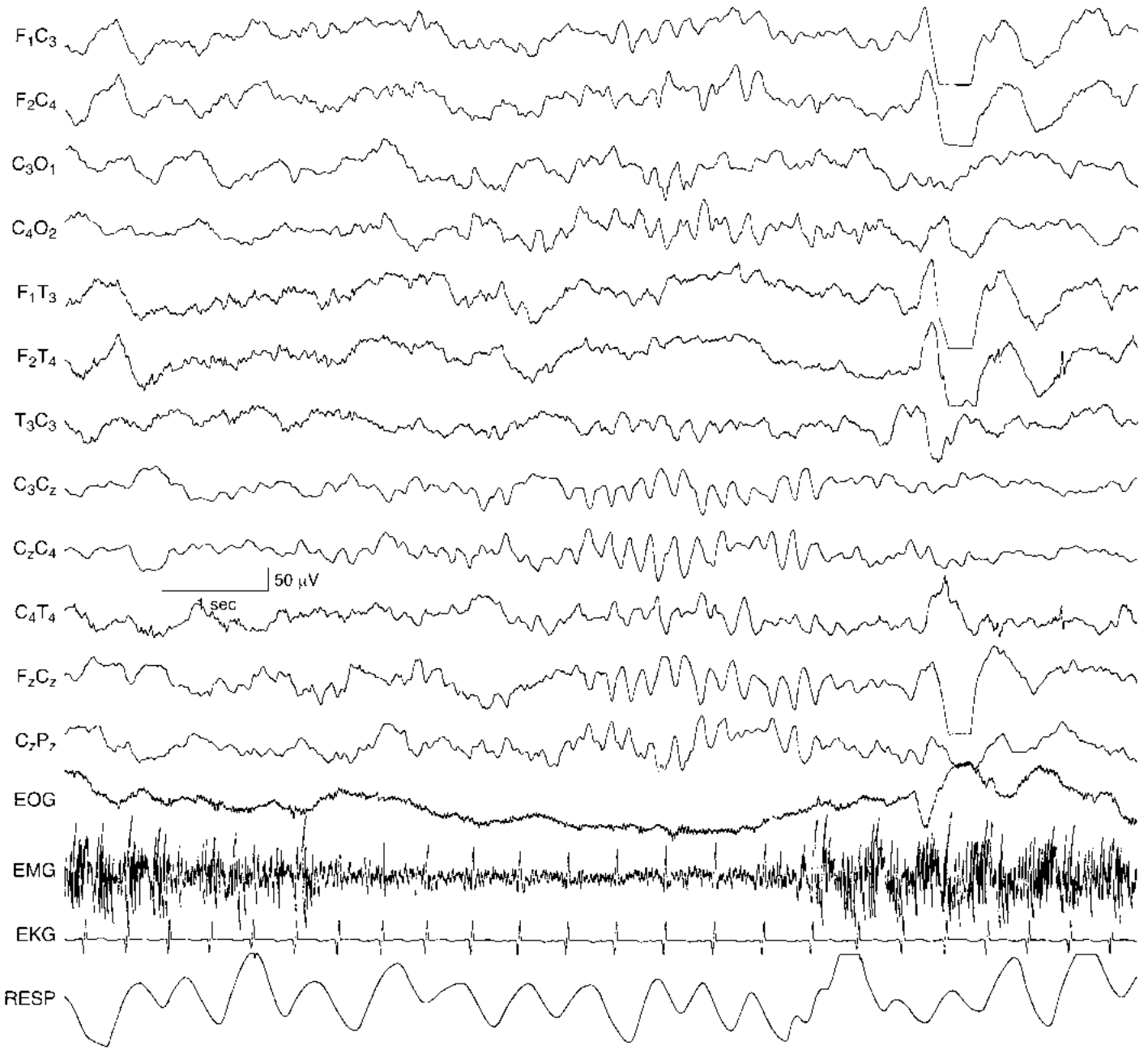

Figure 5.11 Brief burst of rhythmic theta activity in the midline central region. There is a brief burst of rhythmic theta activity in the midline central (Cz) region in this sample from a 40-week CA infant with normal background EEG activity.

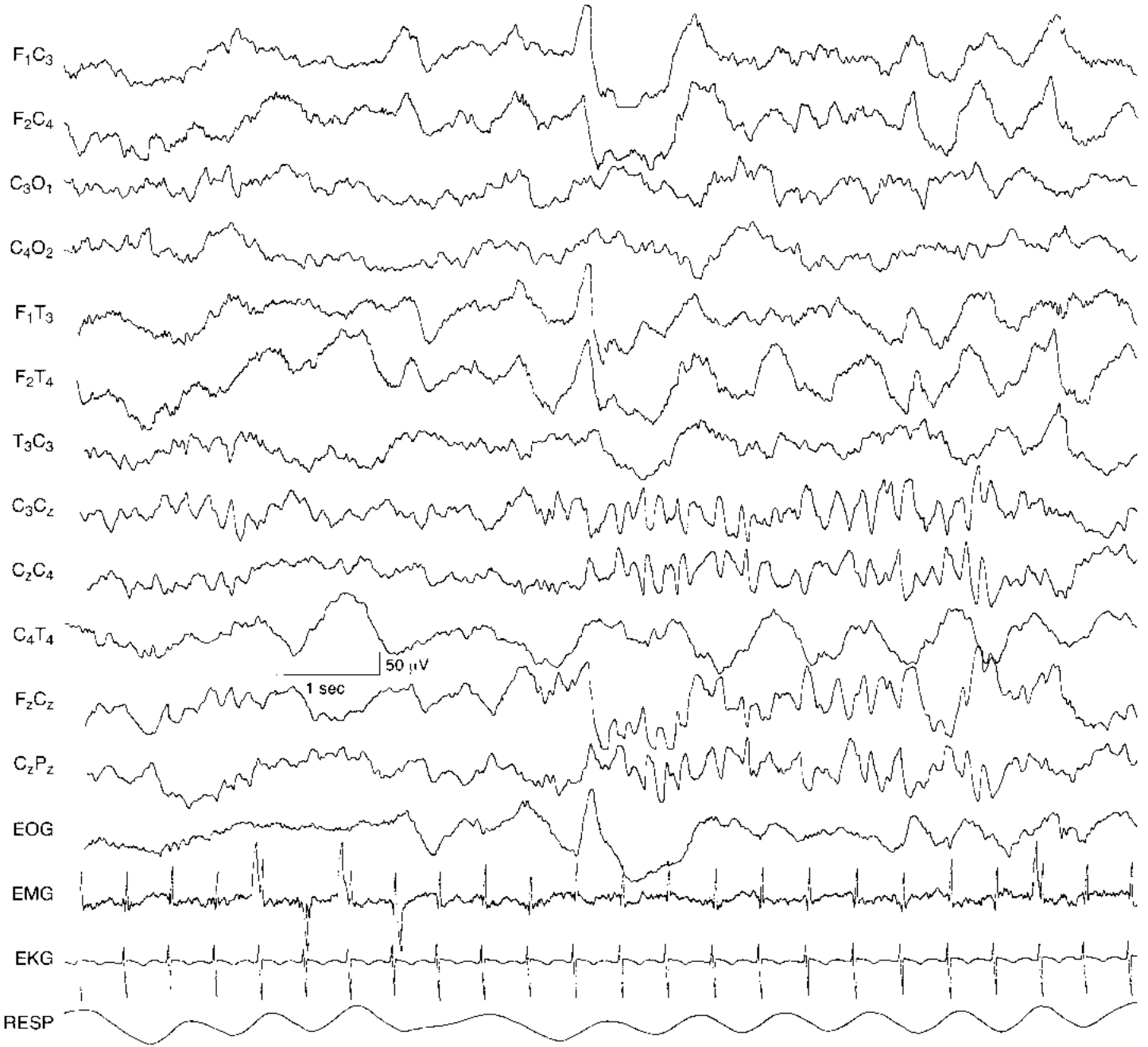

Figure 5.12 Sustained burst of rhythmic theta activity in the midline central region. There is a sustained burst of rhythmic theta activity in the midline central (Cz) region. Normal frontal sharp transients are present. The background EEG activity is normal in this 40-week CA infant.

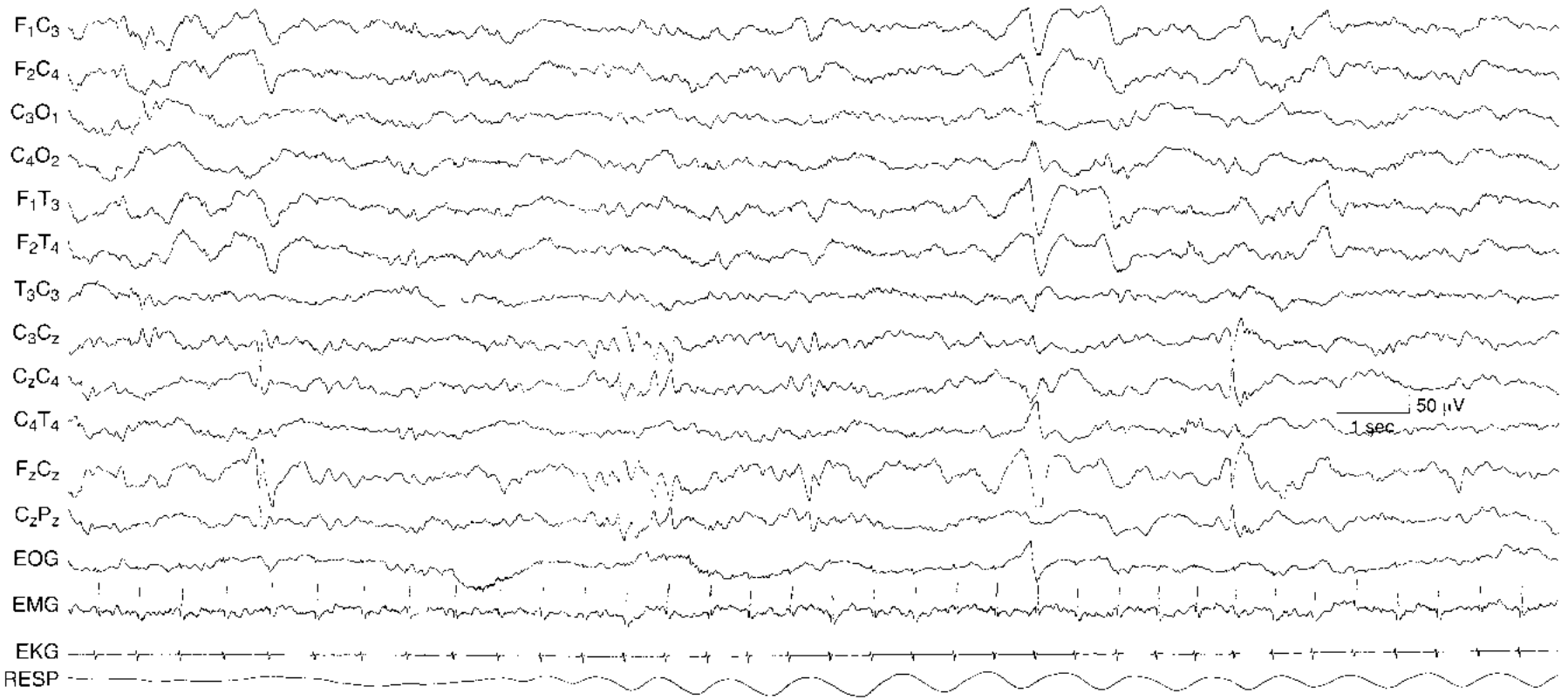

Figure 5.13 Rhythmic midline central theta bursts and midline central sharp waves. There is a brief run of rhythmic theta activity in the midline central region in the middle portion of this sample. Earlier and later there are sharp waves or spikes in the same region that are more abnormal features. Frontal sharp transients, normal waveforms, are present and the EEG background activity is normal in this 40-week CA infant.

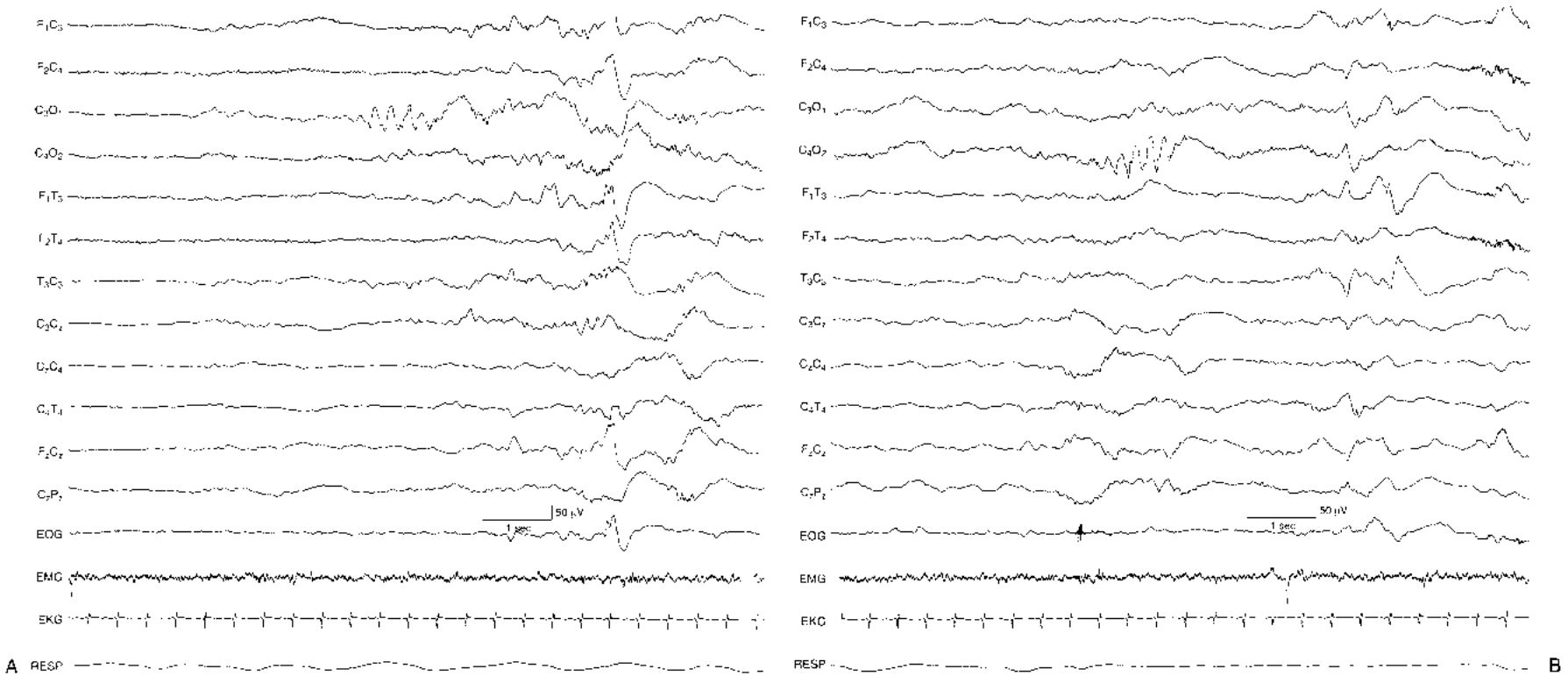

Figure 5.14 (A) and (B) Brief, rhythmic occipital theta activity on the left and right. There are brief bursts of rhythmic theta activity in the left **(A)** and right **(B)** occipital regions on two samples from one EEG recording in this 34-week CA infant.

Figure 5.15 Brief, rhythmic occipital theta activity on the left. A brief burst of rhythmic theta activity is present in the left occipital region in the recording from this 40-week CA infant with a normal background EEG.

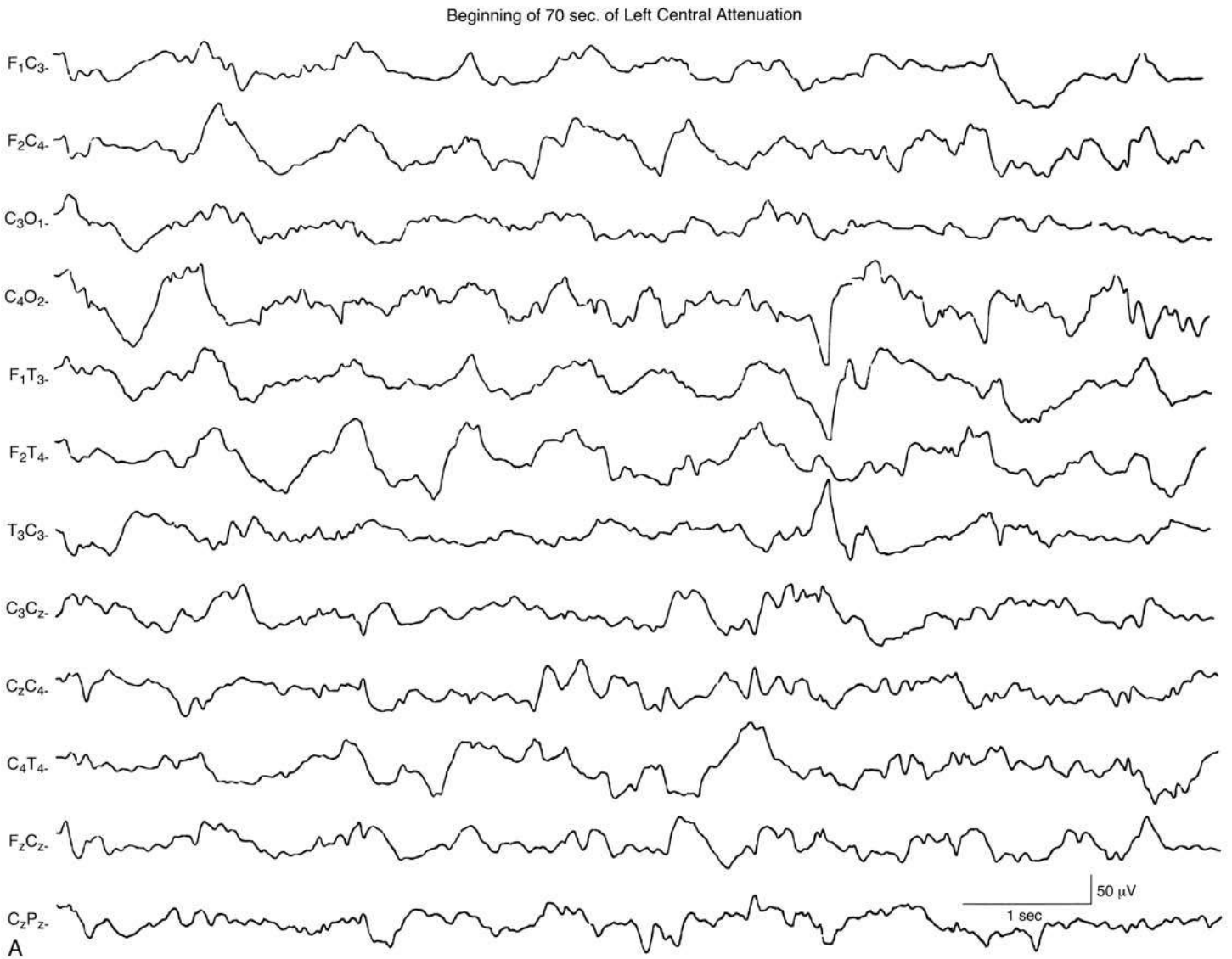

Figure 5.16 (A)–(D) Transient unilateral attenuation of background activity during sleep. Selected segments are shown of an episode of transient unilateral attenuation of background activity during sleep lasting 70 sec. **(A)** Initially, there is voltage attenuation of activity in leads from the left hemisphere. (*continued*)

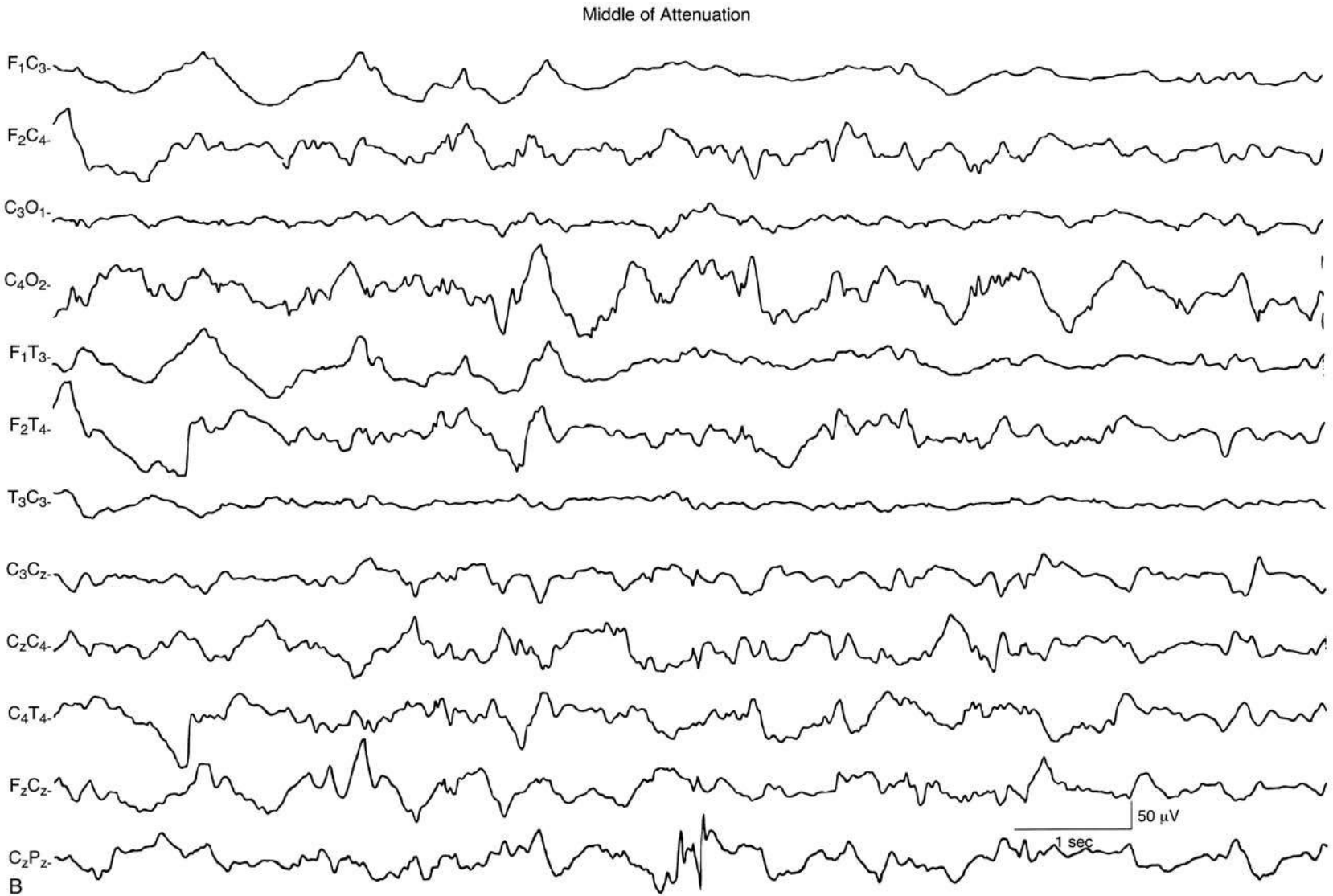

Figure 5.16 (*continued*) **(B)** The attenuation persists for several seconds. (*continued*)

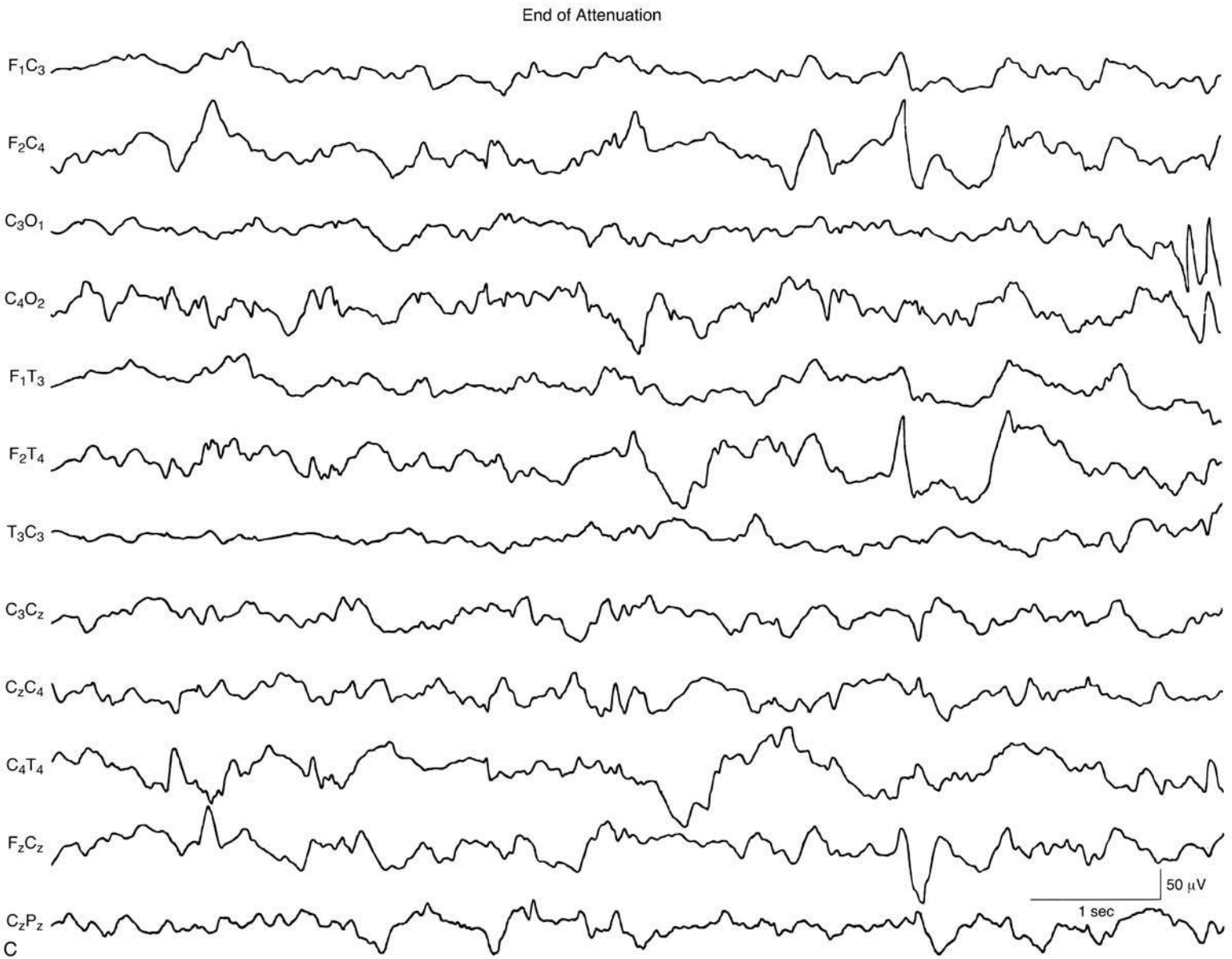

Figure 5.16 (*continued*) **(C)** There is gradual resolution of the attenuation. (*continued*)

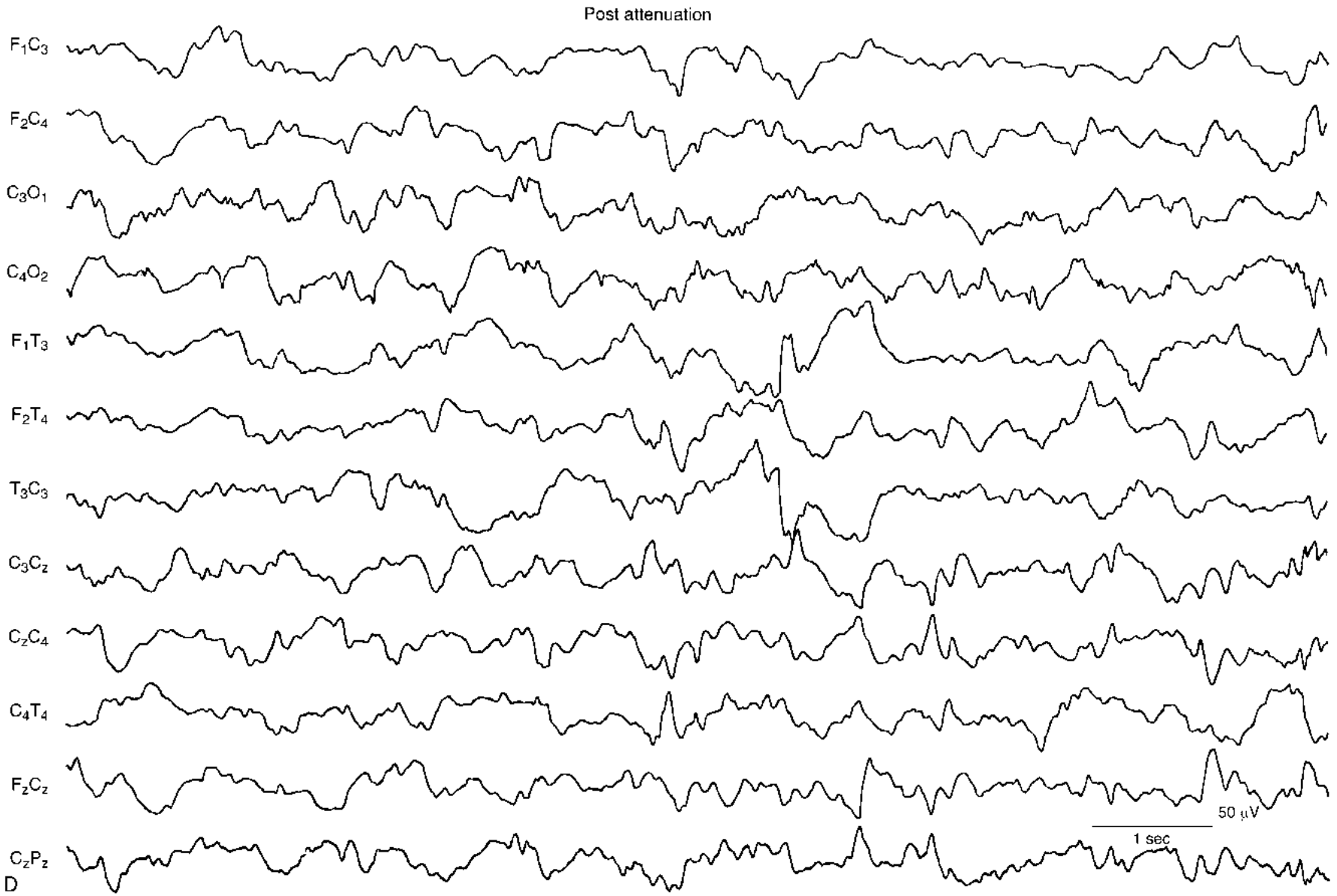

Figure 5.16 (*continued*) **(D)** The EEG eventually returns to baseline. The background EEG activity is normal in this 40-week CA infant.

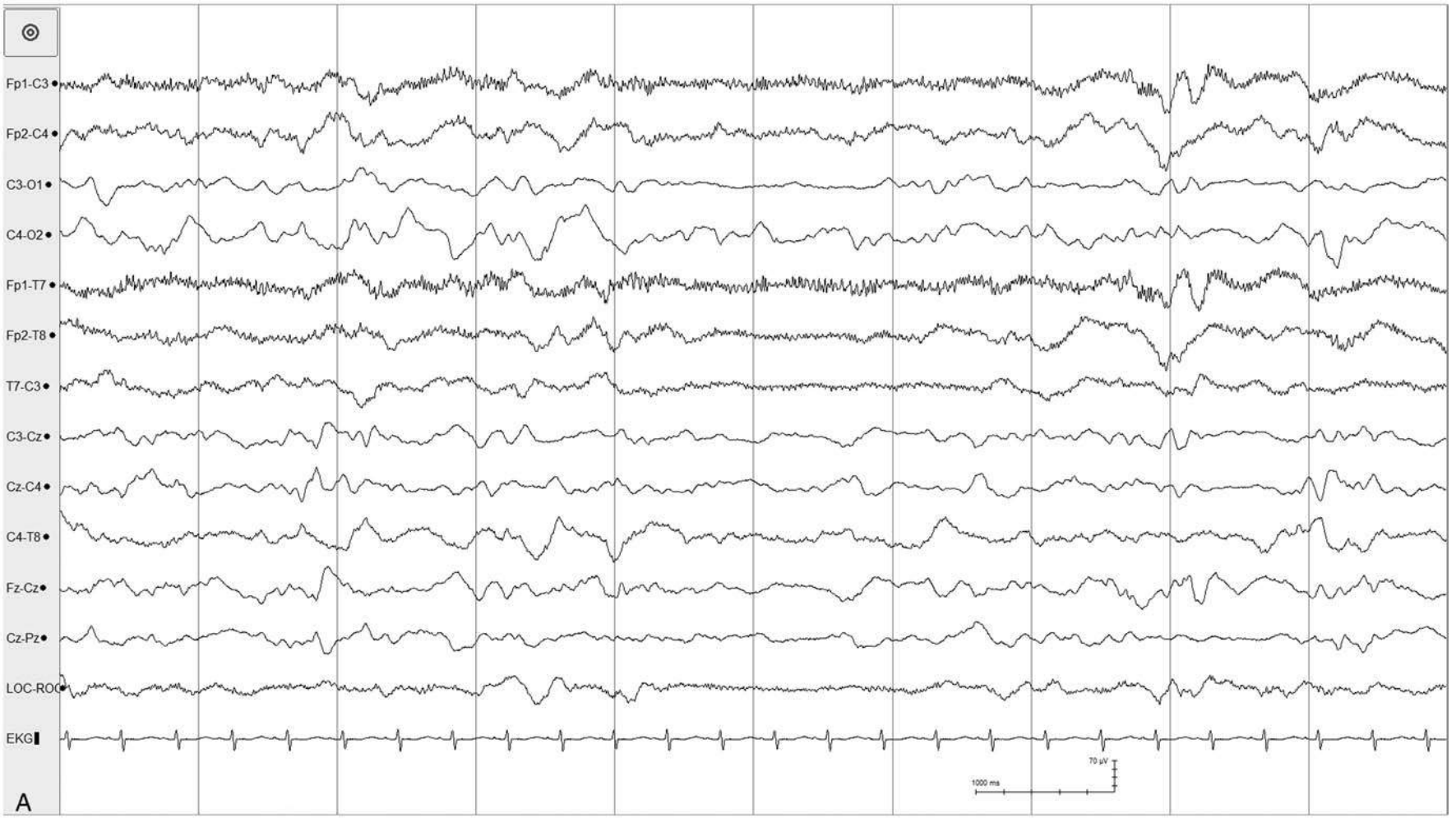

Figure 5.17 (A)–(E) Transient unilateral voltage attenuation. (A) Onset of voltage attenuation in the left posterior central region. (*continued*)

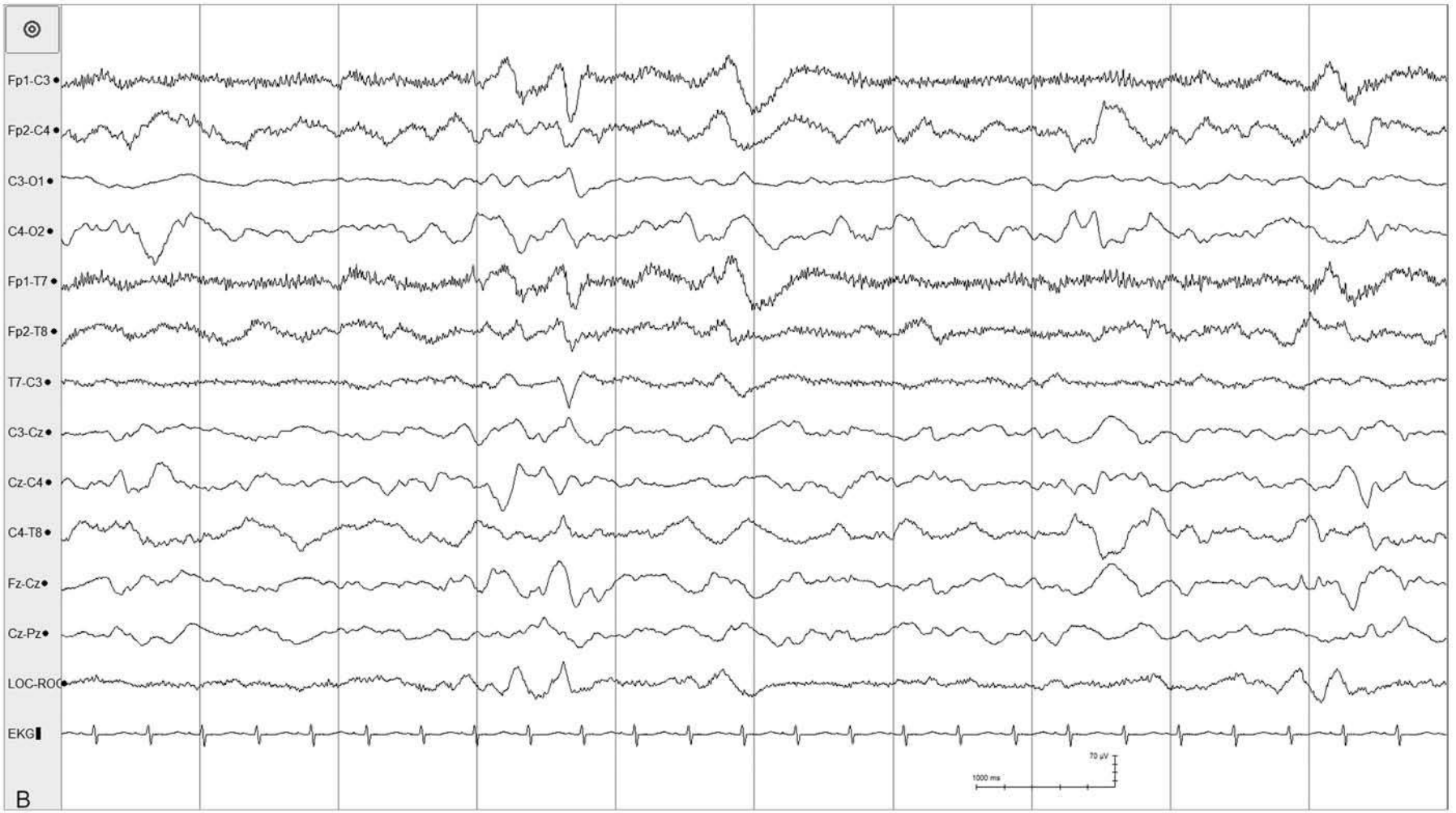

Figure 5.17 (*continued*) **(B)** The voltage attenuation is sustained. (*continued*)

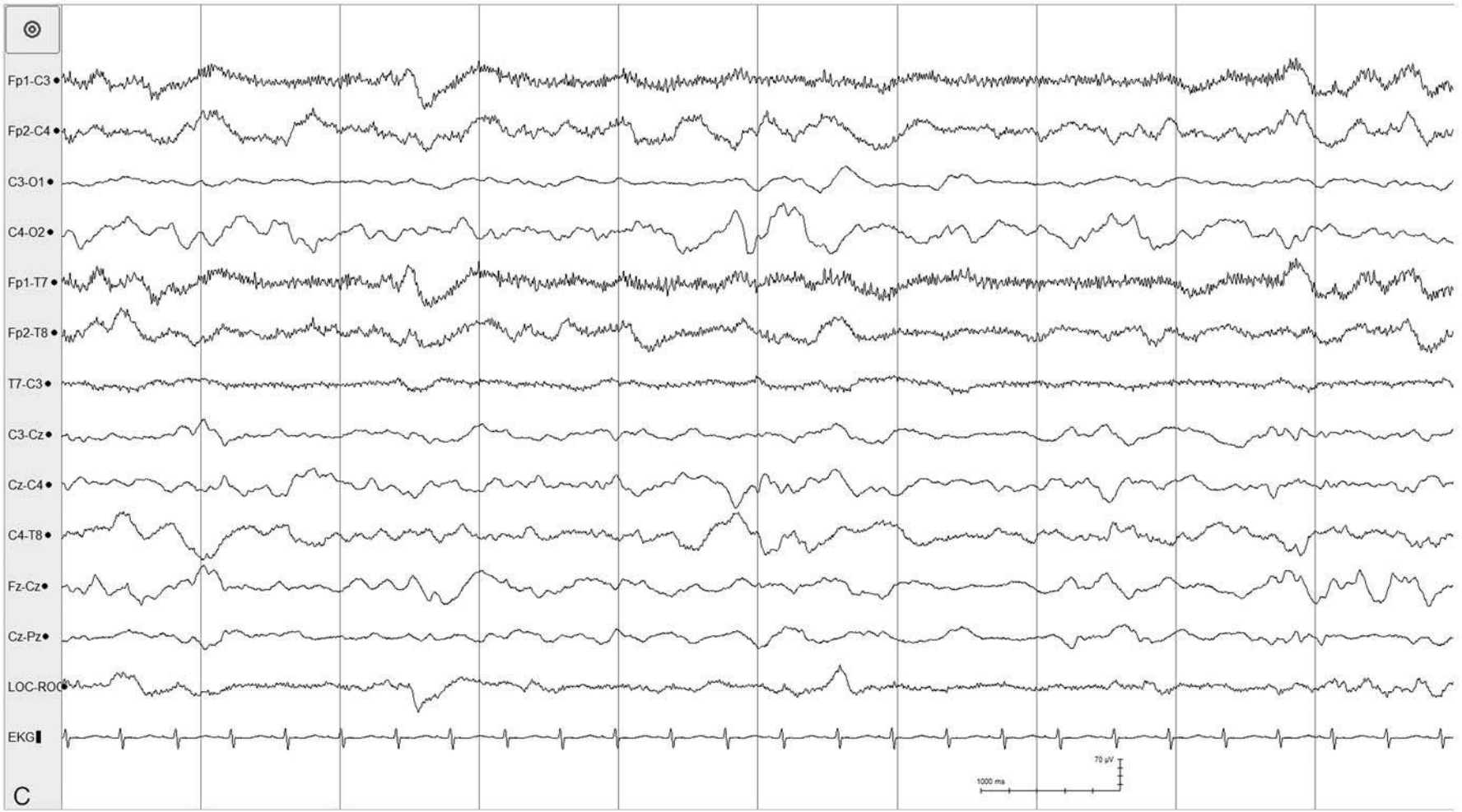

Figure 5.17 (*continued*) **(C)** The voltage attenuation persists. (*continued*)

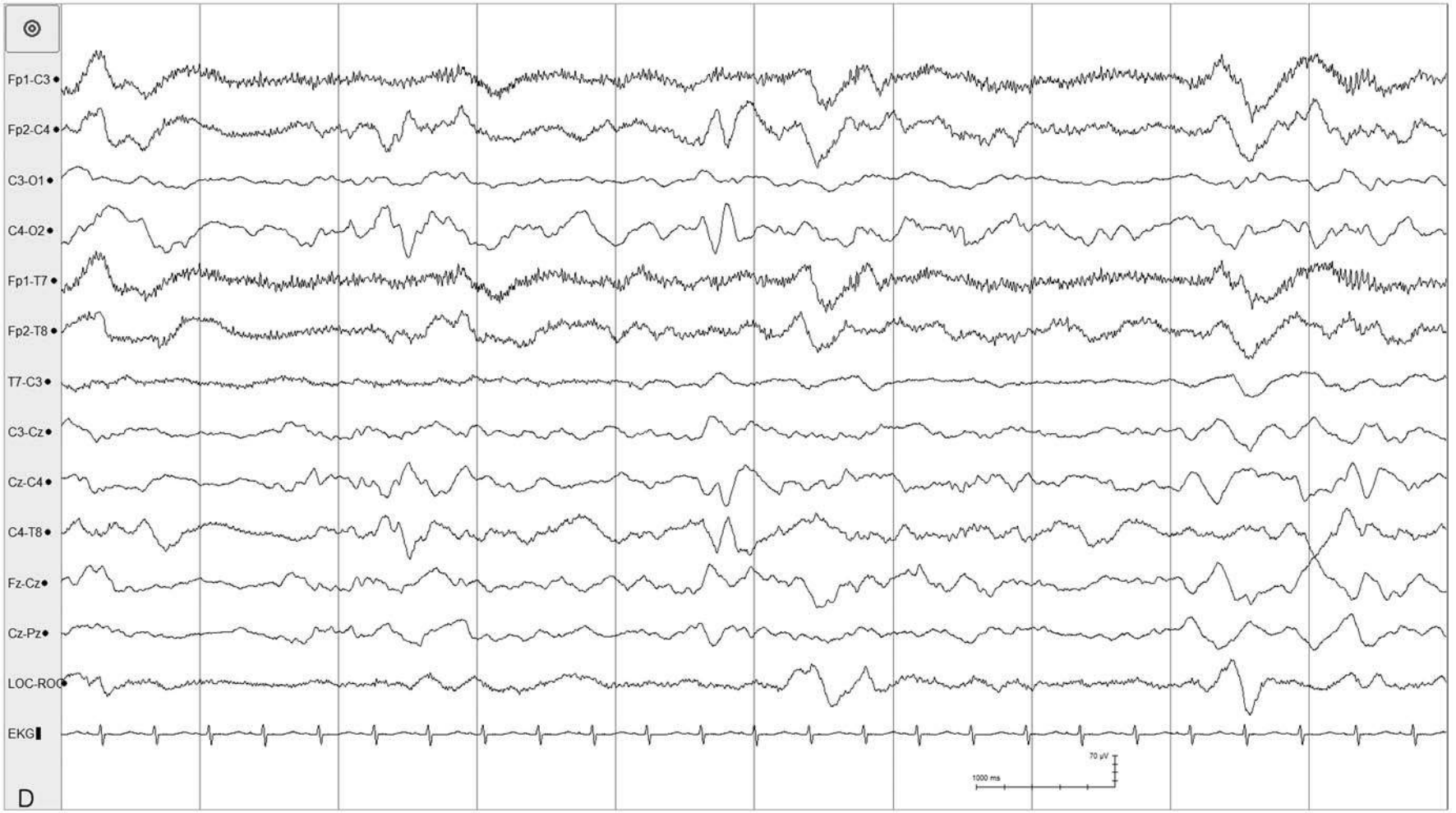

Figure 5.17 (*continued*) **(D)** The voltage attenuation persists. (*continued*)

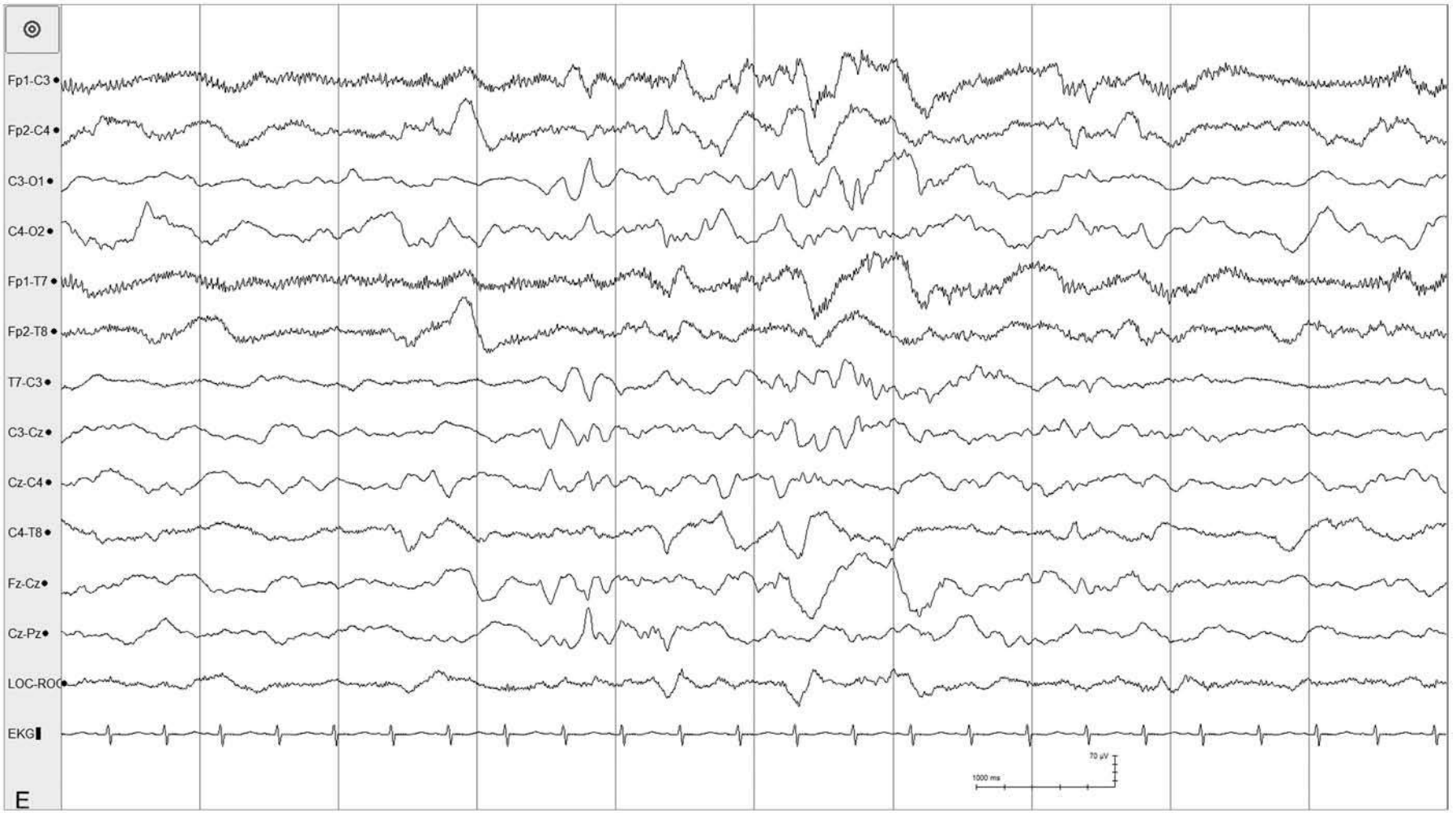

Figure 5.17 (*continued*) **(E)** The unilateral attenuation resolves spontaneously approximately 90 seconds after onset. This occurred in a 40-week CA, 10-day old infant with an otherwise normal background EEG.

CHAPTER 6

EEG Abnormalities of Premature and Full-Term Neonates

THE TIMING OF EEG STUDIES

Ideally, the initial electroencephalogram (EEG) examination should be done within the first 24 hours after birth or after a suspected brain insult. The best estimate of the degree of damage or dysfunction can be made when the EEG documents the evolution of the abnormality over time. Typically, as time passes, the degree of abnormality lessens. The slower this change, the more severe the underlying brain abnormality. If serial studies document the rate and character of the changes, the prognostic information will be more reliable than that obtained from a single study (Briatore et al., 2013; Chequer et al., 1992; Douglass et al., 2002; Graziani et al., 1994; Hellström-Westas and Rosén, 2005; Holmes and Lombroso, 1993; Holmes et al., 1982; Klinger et al., 2001; Kumar et al., 1999; Le Bihannic et al., 2012; Menache et al., 2002; Pressler et al., 2001; Selton and Andre, 1997; Selton et al., 2010; Takeuchi and Watanabe, 1989; Tharp 1990; Tharp et al., 1989; Watanabe et al., 1999; Zeinstra et al., 2001). Serial studies also afford greater opportunity to detect electrical seizures without clinical signs (Glauser and Clancy, 1992), which themselves may be of prognostic significance (see Chapter 7).

Failure to recognize that EEG findings evolve over time may lead to a less than accurate determination of prognosis. For example, an EEG of an infant might show a suppression-burst pattern on the first day of life, a finding typically indicating the presence of severe brain dysfunction. However, hours later, after the infant's physiological condition has stabilized, the EEG activity may become continuous with relatively normal background activity. Such changes drastically alter statements concerning the prognosis. However, a suppression-burst pattern that is sustained over several days or that changes to a depressed and undifferentiated pattern implies a poor prognosis for recovery of brain function. Failure to recognize the importance of the time course has led to contradictory statements in the literature concerning the prognostic significance of suppression-burst activity.

With this caveat, however, some statements can be made concerning the significance of the first EEG recorded early in the course of neurological illness. In infants requiring intensive care, the EEG findings obtained within the first 24 hours after birth can provide reliable prognostic information (Pezzani et al., 1986; Pressler et al., 2001); an EEG with normal findings on the first day, or with only minimally abnormal findings, reliably indicates a good prognosis unless further brain injury occurs later.

DIFFUSE ABNORMALITIES

Dyschronism: Disordered Maturational Development

An experienced neurophysiologist can usually determine conceptional age (CA) to within 2 weeks between 26 and 33 weeks CA and within 1 week between 34 and 37 weeks CA, based upon expected developmental features (see Chapter 4) (Tharp, 1990). Disordered maturational development is referred to as "dyschronism" and, if present, is an important abnormality of the neonatal EEG (Hrachovy et al., 1990).

External Dyschronism

This term refers to an EEG in which the developmental characteristics in all states are immature for the reported gestational or CA. If the developmental features of an EEG are immature for the stated gestational or CA and the features of the background activity in all states are normal, the following questions must be addressed: Is the age as determined by clinical evaluation overestimated or

are the immature EEG features evidence of delayed maturation? The last explanation suggests that a cerebral insult may have occurred during intrauterine life. A discrepancy of 2 weeks or less between EEG age and estimated CA most likely indicates the presence of a transient central nervous system (CNS) dysfunction. However, discrepancies of more than 3 weeks usually indicate the possibility of persistent CNS dysfunction and are frequently accompanied by other EEG abnormalities, including marked suppression of background activity or multifocal sharp waves.

Internal Dyschronism

This term refers to different maturational characteristics between the EEG during wakefulness and in the deepest stages of nonrapid eye movement (NREM) sleep (**Figures 6.1** and **6.2**). For example, characteristics of the waking EEG might be consistent with a CA of 38 weeks, whereas the background activity during NREM sleep might be consistent with a CA of 34 weeks. If dyschronism of 3 or more weeks occurs between these states, other EEG abnormalities are often present. These abnormalities are usually most apparent in NREM sleep, the state that always shows the least mature characteristics (**Figure 6.3**). Such findings suggest significant brain dysfunction. Therefore, an EEG of any infant should include a period of the deepest stages of NREM sleep.

Transient Maturational Abnormalities

Maturational abnormalities may occur transiently in a newborn experiencing acute and ongoing encephalopathy. Therefore, the prognostic significance of an EEG for which developmental features are immature for the stated CA can be determined only by making serial tracings.

Abnormalities of Background Activity in Diffuse Brain Disturbance

There is no consensus on the classification of background abnormalities of the EEG in the neonate, particularly in considering hypoxic ischemic encephalopathy. Walsh et al. (2011) note that most of the classification systems do agree at the extremes, but that the moderately abnormal findings cause the most controversy in terms of their clinical significance.

Prolongation of Interburst Intervals in Premature Infants

The range of duration of normal interburst intervals is CA dependent (**Figure 6.4**) and, in older premature infants, state dependent (**Figure 6.5**). The longest acceptable single interburst interval duration according to CA has been reported to be 24 weeks CA, 60 seconds (Vecchierini et al., 2003); 26 weeks CA, 46 seconds; 27 weeks CA, 36 seconds (Selton et al., 2000); less than 30 weeks CA, 30 to 35 seconds; 31 to 33 weeks CA, 20 seconds; 34 to 36 weeks CA, 10 seconds; 37 to 40 weeks CA, 6 seconds (Hahn et al., 1989). In general, in considering interburst intervals within an individual record, the longest interval is measured, rather than assessing an average of intervals. Although a prolongation of the interburst interval may be secondary to a CNS insult, it may also be due to the use of sedative medications such as morphine (Young and da Silva, 2000) and sufentanil (Nguyen et al., 2003).

Episodes of Generalized and Regional Voltage Attenuation Associated With Multifocal Sharp Waves in Term Infants

Another finding of diffuse dysfunction in the term infant is the presence of generalized or regional episodes of voltage attenuation (**Figure 6.6**). Although abnormal, this suggests relatively mild diffuse dysfunction compared to other findings listed later. This finding often occurs in the presence of multifocal sharp waves.

Depression and Lack of Differentiation

Depressed beta activity, either focal or diffuse, is often the first manifestation of abnormal cortical function. After hypoxia-ischemia, faster frequencies tend to be depressed or obliterated. Lack of differentiation (i.e., the "undifferentiated EEG") refers to virtual or complete disappearance of the polyfrequency activity normally present (**Figure 6.7**) (Selton and Andre, 1997). A depressed and undifferentiated EEG background often accompanies other abnormalities (**Figure 6.8**). However, in some instances, developmental milestones may persist (**Figure 6.9**). Infants with hypoxic-ischemic encephalopathy may be acutely treated with hypothermia. The EEG may initially be depressed and undifferentiated and may either persist or evolve during the cooling period. This may include emergence of polyfrequencies, multifocal sharp waves, continuity and, at times, electrographic seizures (**Figure 6.10**) (Boylan et al., 2015; Glass et al., 2014; Low et al., 2012; Shah et al., 2014; Wusthoff et al., 2011).

A depressed and undifferentiated EEG in the newborn indicates that a severe brain insult has occurred. Disorders causing such an EEG include profound hypoxia, severe metabolic disorders, infectious processes such as meningitis or encephalitis, and intraventricular hemorrhage (IVH). A depressed and undifferentiated EEG within the first 24 hours after birth that persists signifies a poor prognosis.

Suppression-Burst Pattern

The suppression-burst pattern represents an intermediate degree of diffuse brain disturbance between the depressed and undifferentiated EEG and electrocerebral silence. Activity during the bursts consists primarily of delta and theta frequencies, which, at times, are intermixed with sharp waves. The bursts are separated by periods of marked generalized voltage attenuation or electrocerebral silence (**Figures 6.11–6.19**). Suppression-burst patterns persist unremittingly; no change in the EEG activity is seen during the entire recording and the pattern does not react to painful stimuli. Some infants with the suppression-burst pattern may experience periodic slow myoclonic jerks (**Figure 6.17**). Although typically synchronuous on the two sides, the bursts may appear asynchronously, possibly in association with congenital anomalies of the brain (**Figure 6.18**).

Electrocerebral Silence

Electrocerebral silence represents the ultimate degree of depression and lack of differentiation in the neonate. The transition from a severely depressed and undifferentiated background to one that is isolectric may be difficult to determine (**Figure 6.20**) and serial EEGs may be required to demonstrate a persistent degree of cortical inactivity (**Figure 6.21**). An isoelectric EEG (i.e., "electrocerebral silence") is evidence of severe cortex dysfunction, not that of the brainstem, which, in the infant, may sustain vital functions for prolonged periods in the absence of cortical function. Indeed, prolonged survival may occur in infants whose EEGs continue to show electrocerebral silence (Mizrahi et al., 1985). The finding of electrocerebral silence on EEG in the newborn is not used to support a determination of brain death.

Specialized Generalized Patterns

Hypsarrhythmia

The classical hypsarrhythmic pattern as described by Gibbs and Gibbs (1952) rarely appears before 44 weeks CA. However, one modification of this pattern in the neonatal period is the suppression-burst variant (Hrachovy et al., 1984) **(Figure 6.19)**. The bursts consist of asynchronous, high-voltage slow activity mixed with multifocal spikes and sharp waves. The primary features that distinguish this variant of hypsarrhythmia are the periodicity of the bursts and the high voltage of the activity within the bursts.

Patients with infantile spasms and this variant have a poor prognosis for long-term outcome, regardless of whether the pattern develops in the neonatal period or in later months of life (Maheshwari and Leavons, 1975). In addition, when this pattern does appear in the neonatal period, it is closely associated with the presence of inborn errors of metabolism, most notably nonketotic hyperglycemia.

Holoprosencephaly

The term holoprosencephaly is applied to a spectrum of related cerebral malformations resulting from faulty diverticulation of the prosencephalon. The malformation varies in severity, from arhinencephaly (in which the olfactory bulbs and tracts are absent but the brain is otherwise normal) to alobar holoprosencephaly (in which lobes are not demarcated and the cerebrum is monoventricular, with or without a dorsal cyst). A variety of median facial defects (including cyclopia, orbital hypotelorism, cleft lip, cleft palate, and hypoplasia of the premaxilla) are associated with the cerebral malformations (DeMyer and Zeman, 1963; Yakovlev, 1959).

The EEG findings associated with holoprosencephaly were described by DeMyer and White (1964). They include: (a) multifocal spike and polyspike activity mixed with slow waves; (b) periods of monorhythmic beta-, alpha-, theta-, or delta-frequency activity, occurring singly or in various combinations; (c) asynchrony between hemispheres; (d) isoelectric or relatively low-voltage activity; (e) periodic patterns; and (f) lack of any normal organization (**Figures 6.22–6.24**). These findings occur in various combinations in a single patient. Equally dramatic are the continuous and abrupt changes from one pattern to another, such that within few minutes, most or all of the aforementioned features can be visualized. This constellation of findings is not seen in other disorders of infancy and is therefore diagnostic for holoprosencephaly. Infants with holoprosencephaly often have unusual or stereotyped movements suggestive of seizures. However, there is no correlation between these movements and EEG changes. The prognosis is poor; about 50% of infants die within the first month of life; about 80% will not survive past the first year.

PATTERNS THAT MAY BE FOCAL OR GENERALIZED

Sustained Rhythmic Alpha and Theta Activity

Sustained, rhythmic 4 to 7 Hz activity (theta) and/or 8 to 10 Hz (alpha), 40 to 100 μV activity that is generalized or focal is an abnormal finding. However, precise correlations to specific etiologic factors have not, for the most part, been determined. This activity may occur almost continuously or paroxysmally in brief runs and may occur as theta, alpha, or mixed activity (**Figures 6.25–6.30**).

When alpha activity occurs focally, it is most prevalent in the central or temporal regions, where it may occur independently on the two sides. Although this activity may be most prominent in the awake state, it is usually present in all states and is usually accompanied by other abnormalities such as abnormal sharp waves. Generalized rhythmic alpha activity has been associated with various underlying abnormalities, most commonly congenital heart disease; However, it also may be seen in infants who have received CNS-active drugs such as diazepam and phenobarbital (Hrachovy and O'Donnell, 1999). It is important to distinguish this pattern from the alpha seizure pattern (see Chapter 7).

Sustained Rhythmic Delta Activity

In some instances bifrontal slow (delta) activity is considered an abnormal finding. Abnormal bifrontal slow activity can be differentiated from normal bifrontal slow activity by its presence in all stages of sleep and wakefulness and its unrelenting character (**Figure 6.31**). Abnormal rhythmic slow (delta) activity also may be present in the occipital regions bilaterally (**Figure 6.32**).

FOCAL ABNORMALITIES

Periodic Complexes

Periodic and quasiperiodic discharges in a newborn's EEG have been reported to occur in association with various CNS injuries. They are believed to be suggestive of the presence of neonatal herpes simplex virus encephalitis (HSVE) (Mikati et al., 1990; Mizrahi and Tharp, 1982) (**Figure 6.33**). While such periodic discharges may be associated with HSVE, some may also be interpreted as electrical seizures of the depressed brain type (see Chapter 7). In addition, periodic discharges are not, however, peculiar to HSVE and may occur with various other CNS insults such as infarction (Randò et al., 2000; Scher and Beggarly, 1989).

Unilateral Depression of Background Activity

Mild shifting asymmetry of the background EEG activity between hemispheres is a common finding in the newborn, particularly during NREM sleep. However, an abnormal finding is a marked voltage asymmetry of background rhythms between hemispheres that persists in all states (**Figures 6.16** and **6.34–6.36**). Unilateral depression may occur in association with a wide range of structural cerebral lesions such as infarction, hemorrhage, focal cystic lesions, and rarely, congenital malformations. In addition, other intracranial abnormalities such as subdural fluid collections may be associated with this EEG finding. However, focal depression of the background activity may also persist for variable periods after electrical seizures. A marked asymmetry of the background activity may also result from nonintracranial causes such as subgaleal swelling, scalp edema, or technical error.

Focal Slow Activity

Just as in older infants, the finding of focal slow activity that persists at a specific site may indicate the presence of a focal destructive lesion such as infarct, hemorrhage, or, more specific to neonates, congenital anomalies of the brain (**Figure 6.37**).

Central Positive Sharp Waves

These waves are 50 to 250 μV surface-positive transients lasting 100 to 250 ms and occurring either unilaterally or bilaterally in the central regions (**Figures 6.38–6.40**). A lower voltage after-going surface-negative component may be present. The waves usually occur singly or in brief runs. Central positive sharp waves are not epileptiform discharges, and the physiological processes causing them remain unknown. They have been described most notably in infants with IVH (Blume and Dreyfus-Brisac, 1982; Cukier et al., 1972; Lomboso, 1982; Tharp et al., 1981), and white matter necrosis (periventricular leukomalacia) (Lombroso, 1982; Marret et al., 1986; Novotny et al., 1987). They have also been associated with "major ultrasound lesions" such as grade III IVH, periventricular hemorrhagic infarction, cystic periventricular leukomalacia, persistent periventricular echodensities, and persistent ventricular dilatation (Castro Conde et al., 2004). The timing of the recording in relation to the occurrence of the hemorrhage may influence their appearance (Clancy and Tharp, 1984; Kidokoro et al., 2009). Current thought is that the finding of central positive sharp waves is not specific for IVH but rather for white matter necrosis, which may result from a variety of insults, including IVH (Novotny et al., 1987). In addition, the abundance and rate of recurrence of central positive sharp waves within a single record of an infant appear to correlate with long-term neurological outcome; a rate of greater than 2 per second has been associated with a poor outcome (Blume and Dreyfus-Brisac, 1982; Kidokoro et al., 2009; Nosralla et al., 2009). Other conditions such as meningitis, hydorcephalus, amino-aciduria (Tharp, 1980), and asphyxia (da Costa and Lombroso, 1980) have also been associated with central positive sharp waves.

Temporal Sharp Waves

The problems of determining whether sharp waves that occur in the temporal regions are normal or abnormal have been previously discussed (see Chapter 5). Whereas some sharp waves occurring in the temporal regions are considered normal, others may not meet the criteria to be called abnormal and are thus of questionable significance. However, there are temporal sharp waves that are clearly abnormal. Criteria for abnormality include morphology, polarity, rate of recurrence, and persistence at one site (**Figures 6.41–6.44**). They may be, although not always, associated with focal injury in the region of occurrence. They are not considered to be interictal epileptiform findings (see Chapter 7).

Extratemporal Focal Sharp Waves

Abnormal sharp waves that appear as slow sharp transients or rapid spikes may occur in the frontal (**Figures 6.45–6.51**), central, (**Figures 6.52–6.54**) and occipital (**Figures 6.55–6.57**) regions. When persistently focal, they may suggest focal brain injury, although often no well-defined structural lesion can be documented by neuroimaging.

Multifocal Sharp Waves

As already noted, sharp waves in the newborn EEG are common, with certain sharp-wave activity being considered "normal." Multiple foci of high-voltage, long-duration, sharp-wave activity are commonly seen in infants who have experienced a diffuse CNS insult (**Figures 6.58–6.61**). Such abnormal sharp waves usually predominate in the temporal regions and may persist over one hemisphere. As noted, multifocal sharp waves usually accompany various other EEG abnormalities, including depressed and undifferentiated background activity, episodes of attenuation, and rhythmic bifrontal delta activity. Multifocal sharp waves may be the only abnormality after a CNS insult and may also be the last remaining evidence of CNS dysfunction in serial tracings. This abnormality is usually maximal in NREM sleep, and in some infants it may occur only in this state (**Figure 6.3**). Multifocal sharp waves cannot be used as evidence that a seizure has occurred or will occur, because the sharp waves do show a significant association with neonates with seizures.

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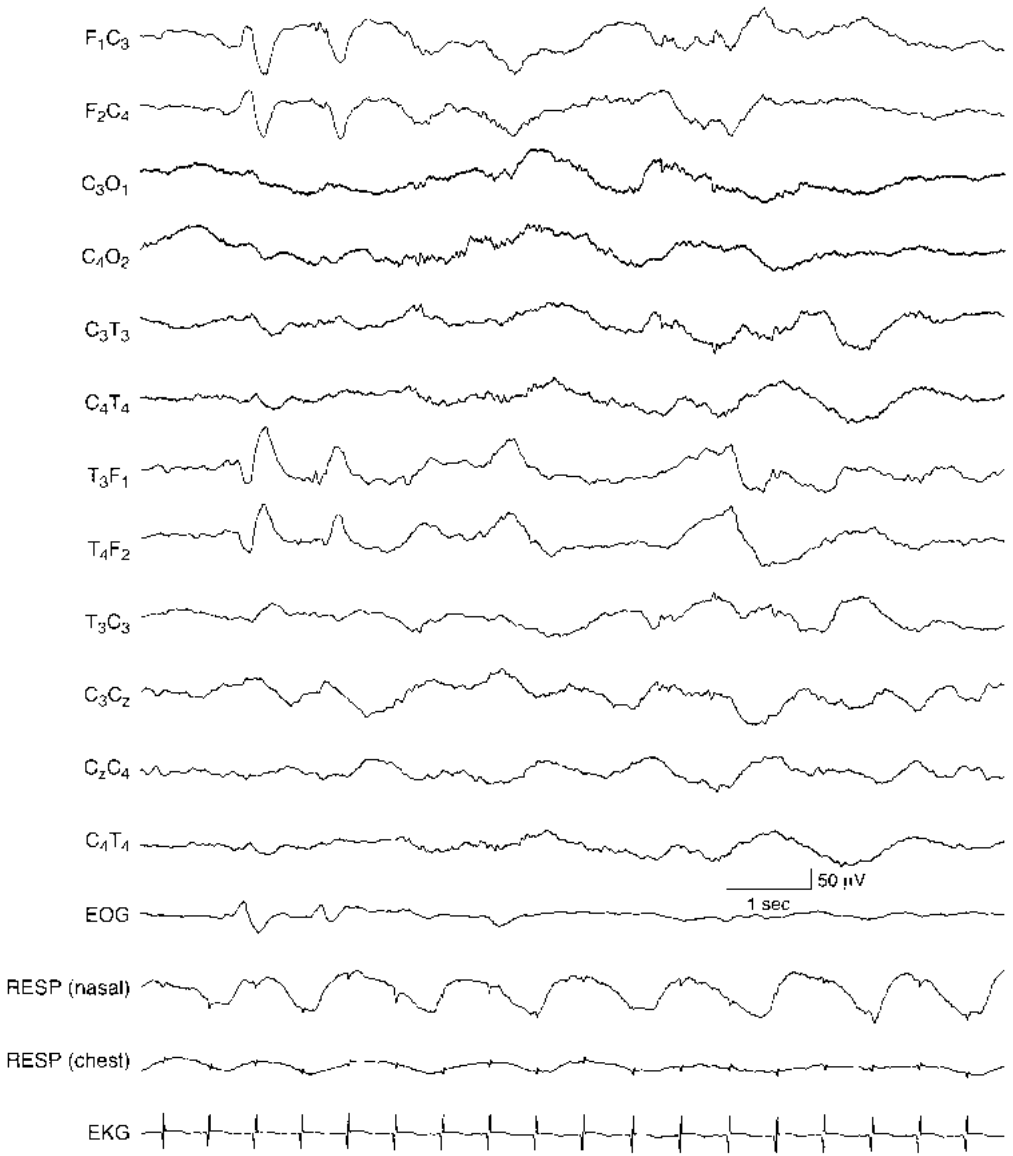
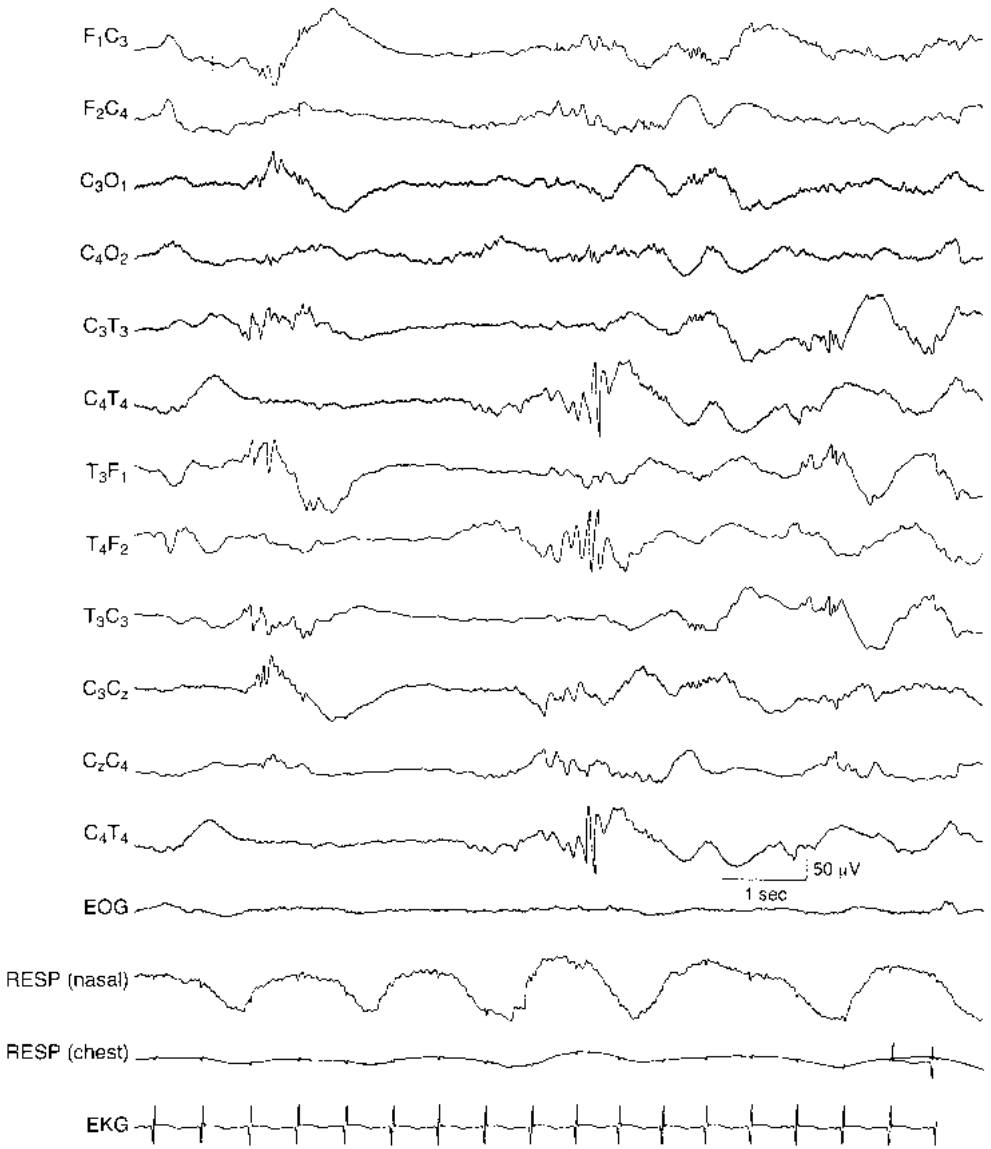


Figure 6.1 (A) and (B) Internal dyschronism. (A) Transitional sleep, 38 to 40 weeks CA. The developmental features of the EEG in this term infant in transitional sleep are consistent with a conceptional age of 38 to 40 weeks and are within the range of normal variation. (*continued*)



B

Figure 6.1 (*continued*) **(B)** In deep NREM sleep, during the same recording of the infant, the developmental features of the EEG are consistent with the CA of 33 weeks, with central beta–delta complexes and temporal alpha bursts. This NREM sleep recording is also without abnormalities.

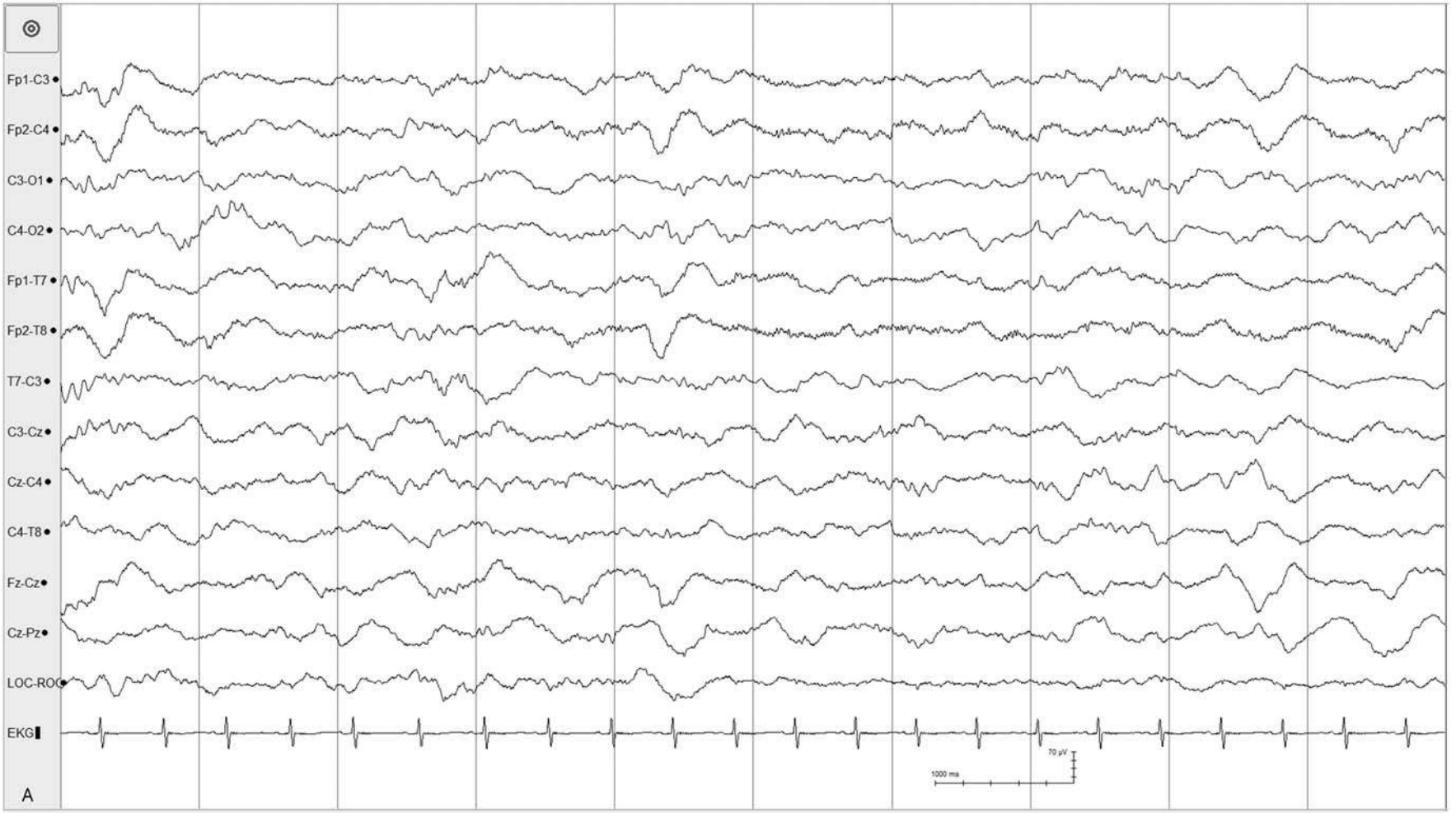


Figure 6.2 (A)–(C) Internal dyschronism. (A) The awake EEG is characterized by continuous polyfrequency activity consistent with the stated conceptional age of 39 weeks. (*continued*)

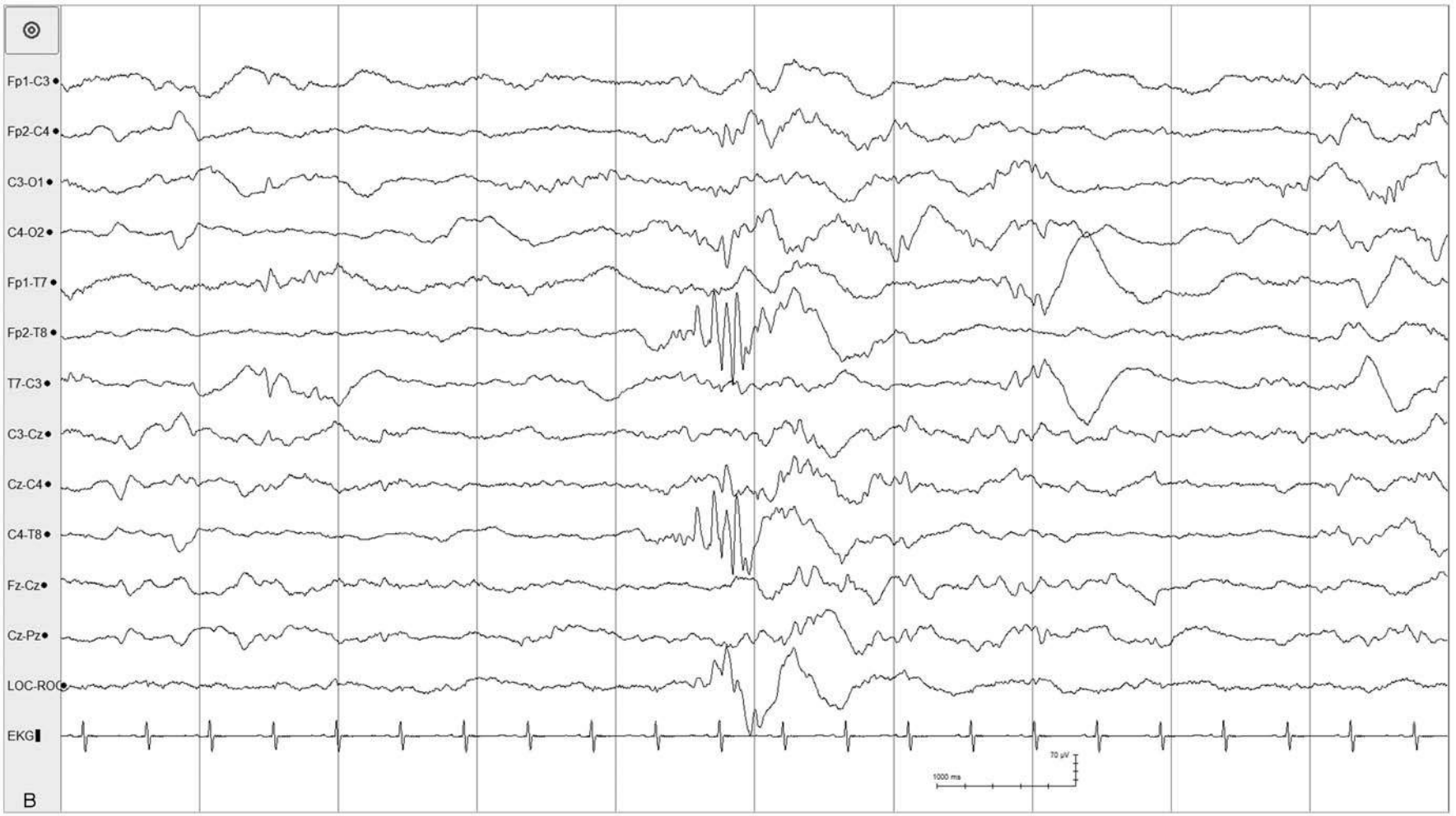


Figure 6.2 (*continued*) **(B)** The EEG in the same infant during sleep is consistent with a CA of 32 to 33 weeks. The background is discontinuous with some asynchrony. There is a temporal alpha burst and beta–delta complexes. (*continued*)

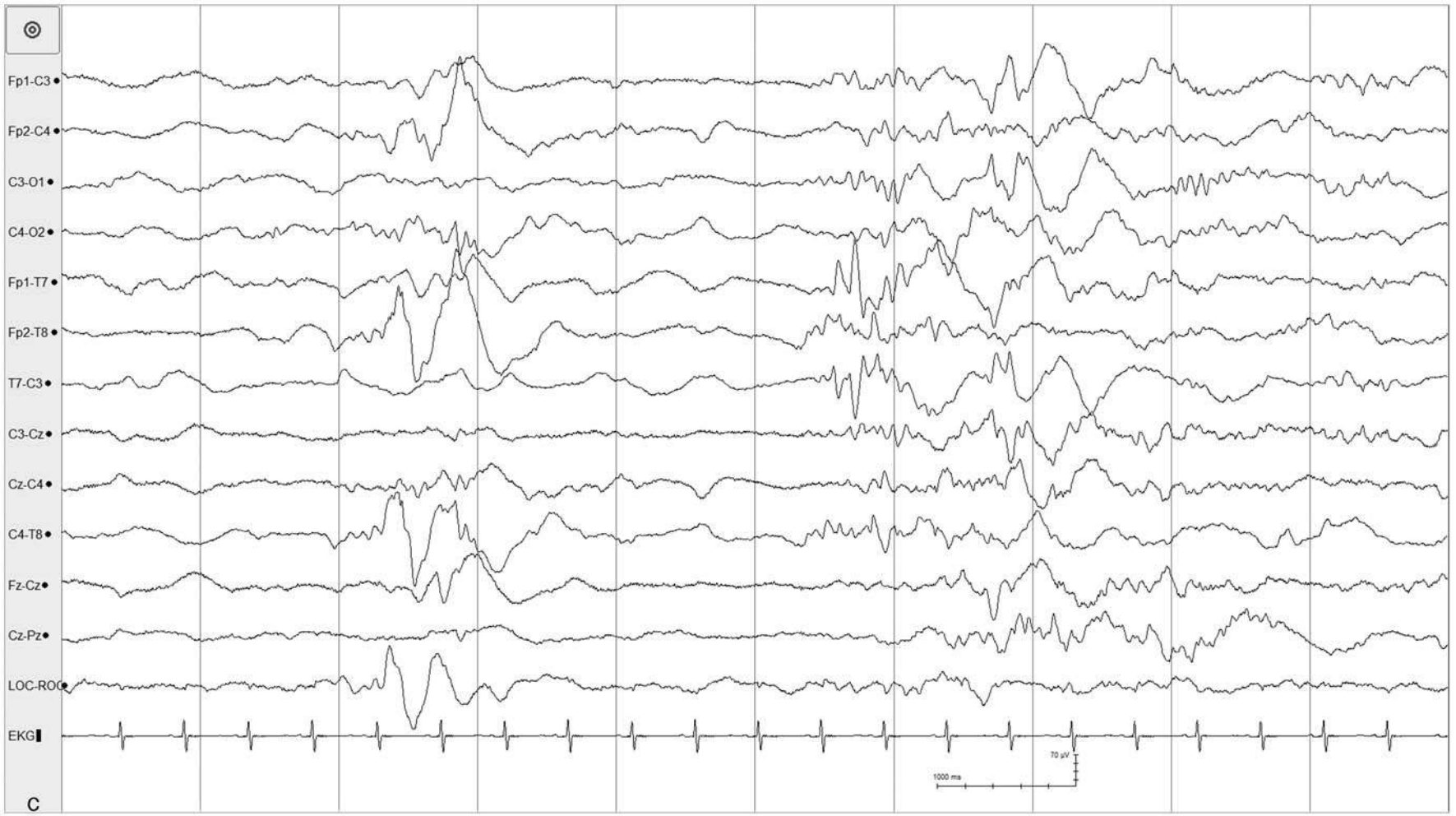


Figure 6.2 (*continued*) **(C)** Further discontinuity, asynchrony, and a temporal theta burst and beta–delta complexes. This infant had MRI findings of simplified gyral pattern, focal polymicrogyria, delayed myelination, and evidence of small lacune focal intrauterine ischemic insult.

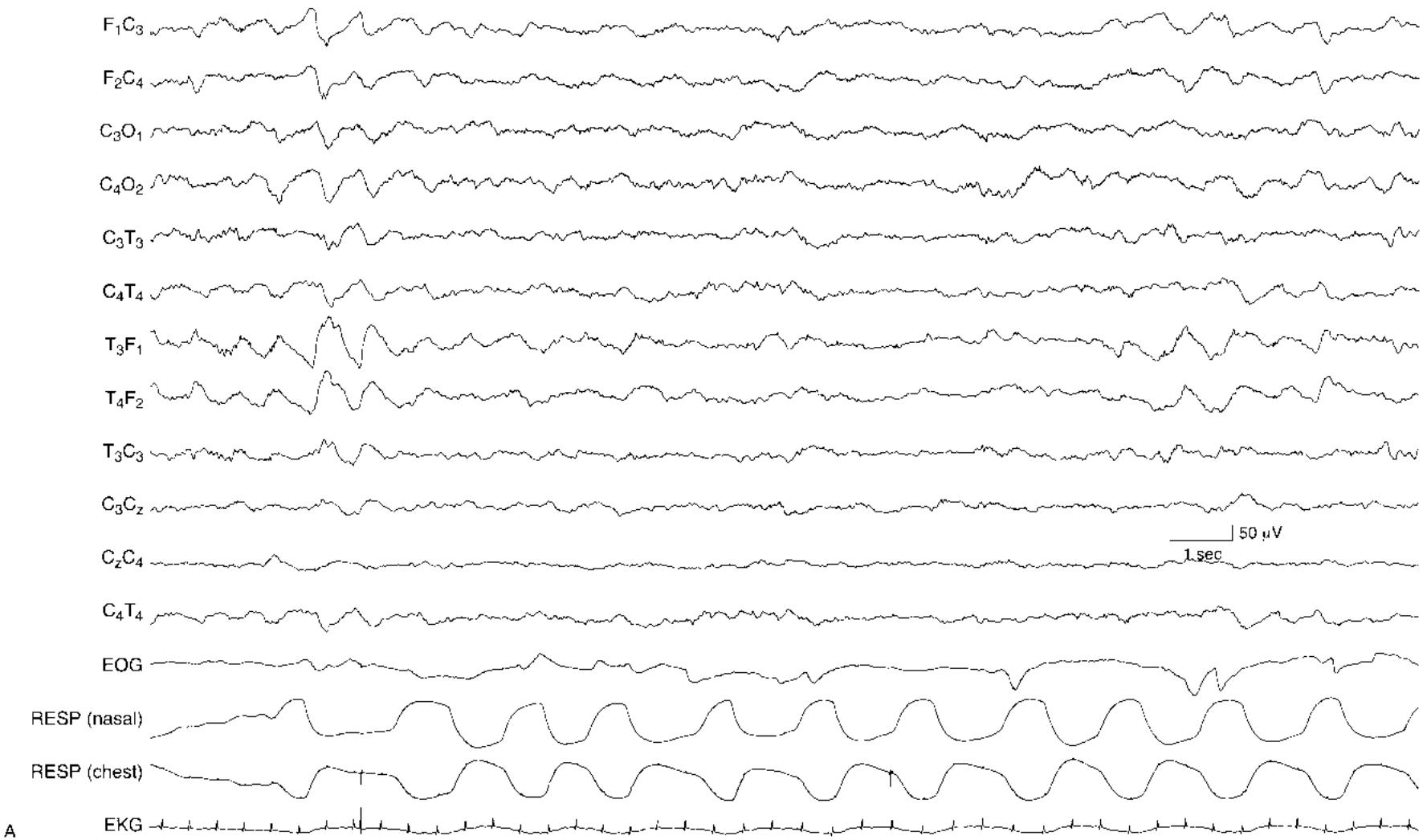


Figure 6.3 (A) and (B) Internal dyschronism with state-dependent abnormality on the EEG. (A) The awake EEG of this term infant, suspected of hypoxic-ischemic encephalopathy, is within the range of normal variation and its developmental features are consistent with that conceptional age. (*continued*)

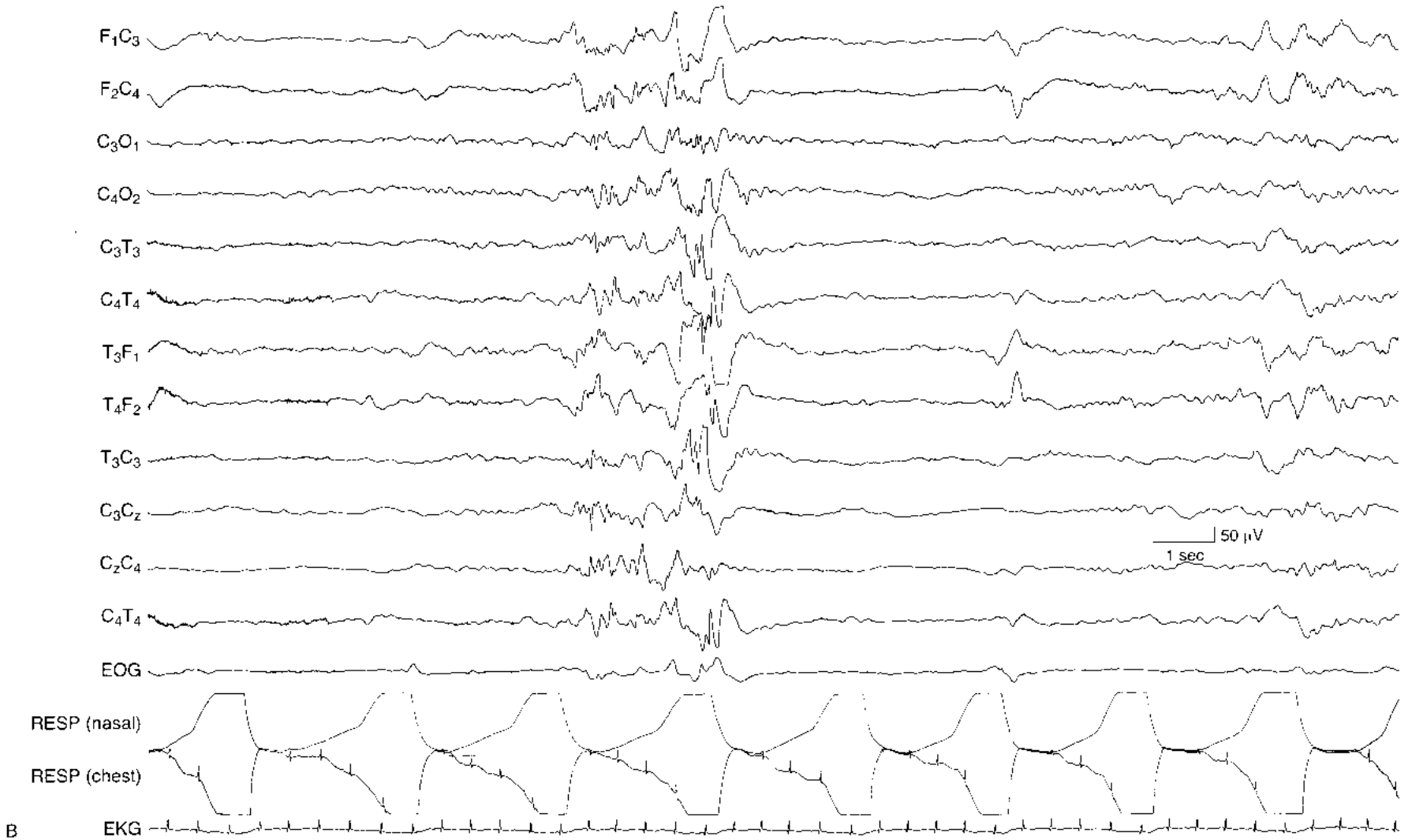


Figure 6.3 (*continued*) **(B)** During NREM sleep, the EEG is abnormal, with excessive discontinuity, asynchronous activity including sharp waves and spikes during periods of bursting, and no well-defined developmental milestones.

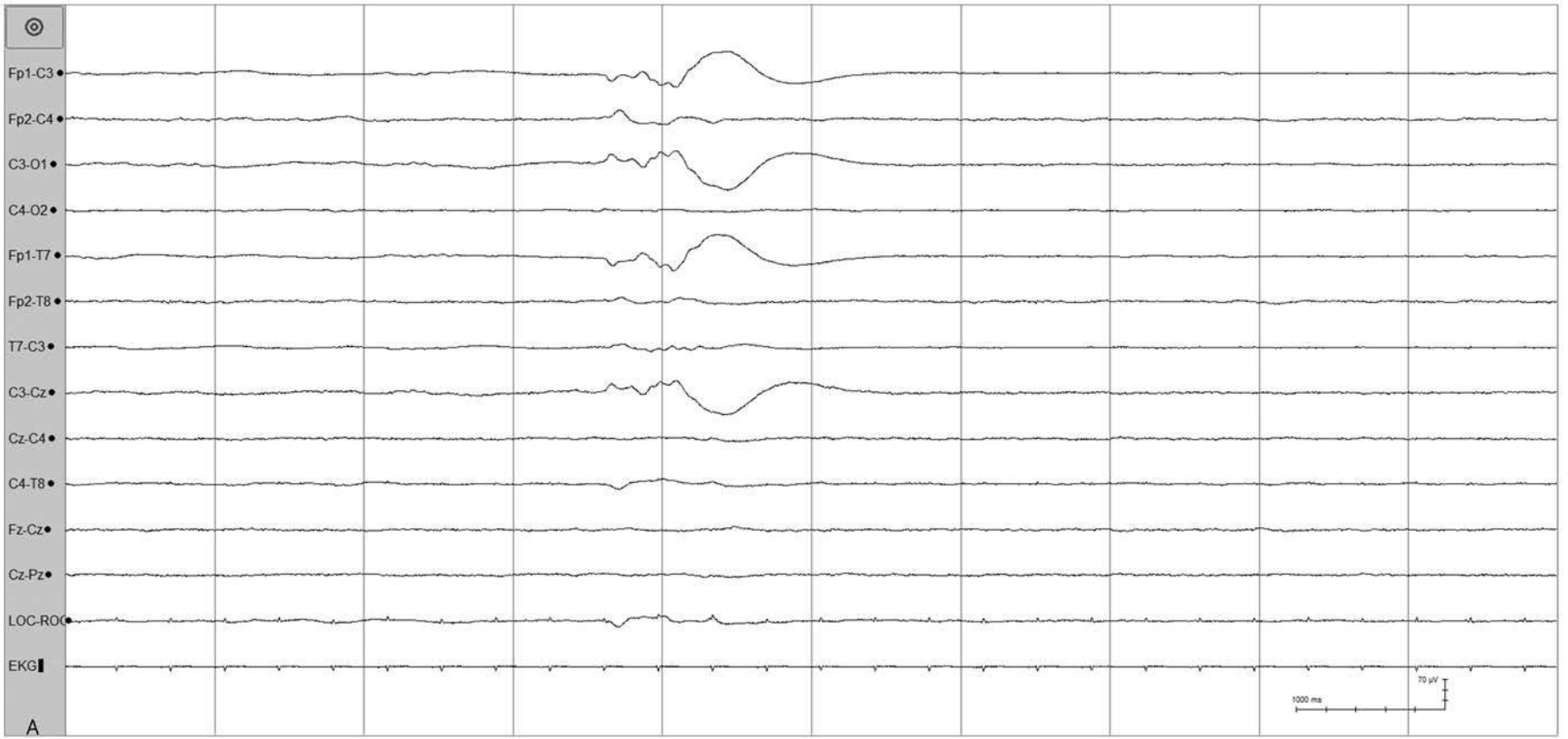


Figure 6.4 (A) and (B) Low-voltage bursting and prolonged interburst interval in prematurity. (A) Low-voltage bursting with relatively brief interburst intervals in a 26-week CA infant. (*continued*)

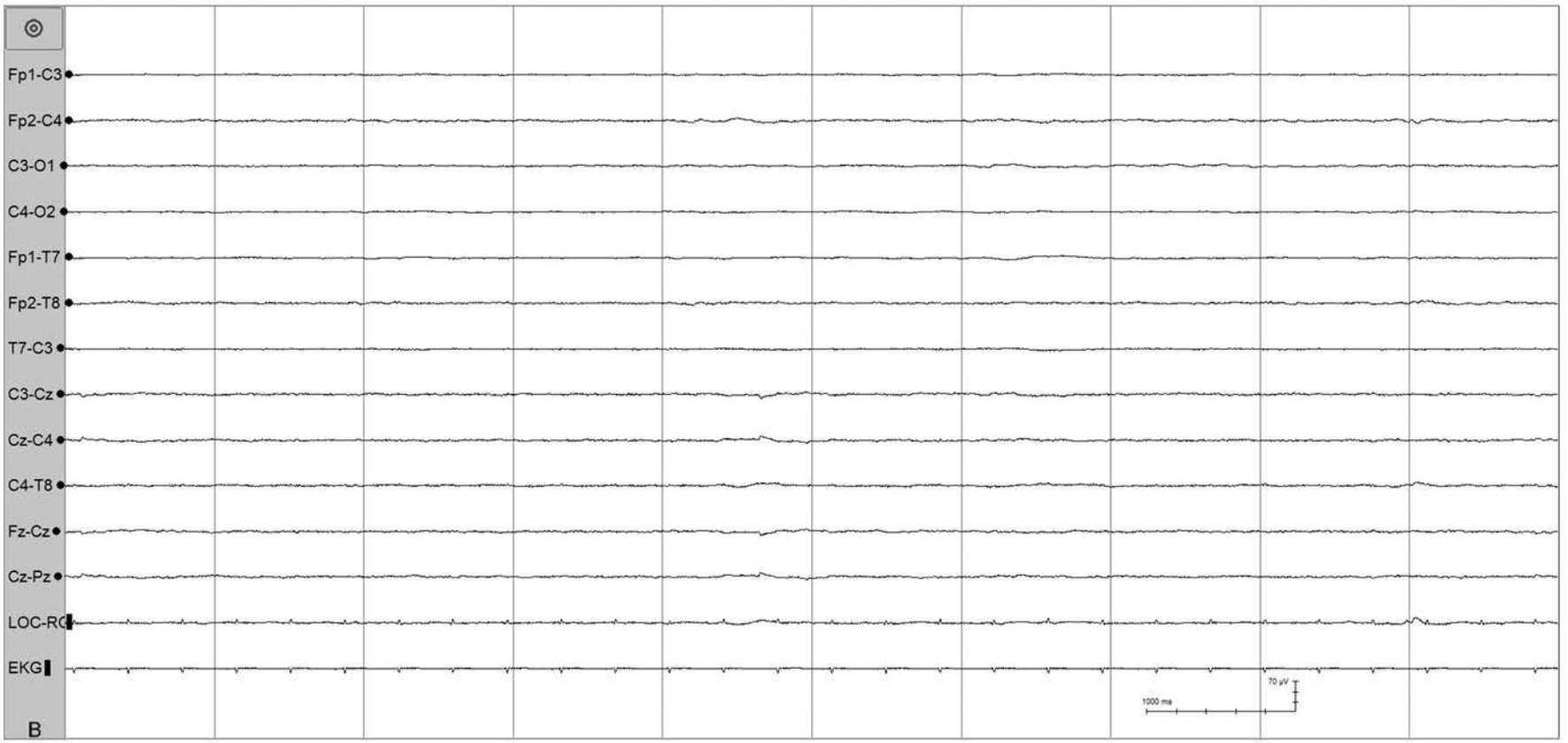


Figure 6.4 (*continued*) **(B)** In the same recording, this is a segment of an interburst interval which eventually lasted 100 seconds.

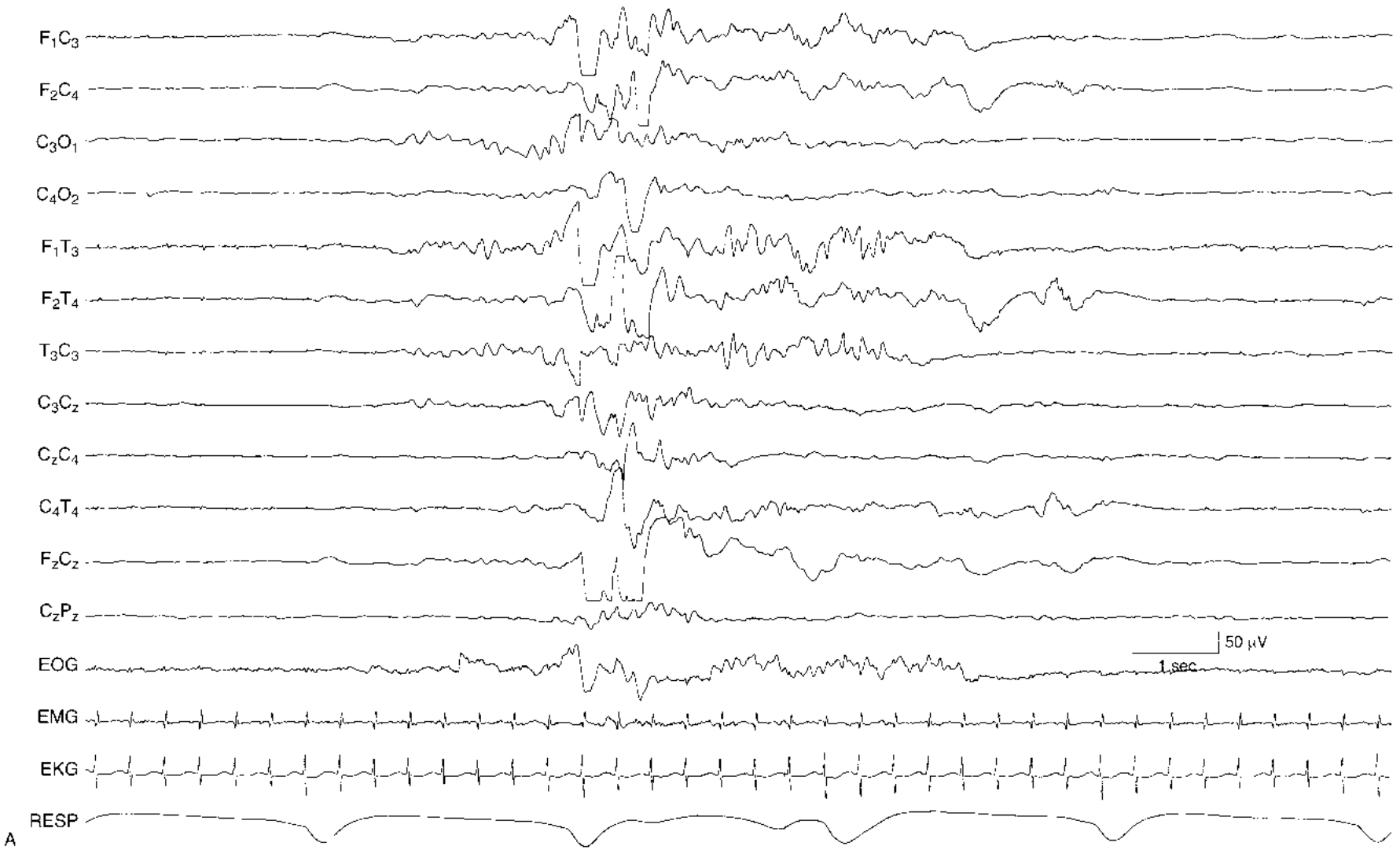


Figure 6.5 (A) and (B) Excessive discontinuity. During NREM sleep, the degree of discontinuity is excessive for the infant's CA of 35 weeks. This is shown in two contiguous segments **(A)** and **(B)**. In addition, there is an absence of beta–delta complexes. This infant was found to have grade III IVH bilaterally. (*continued*)

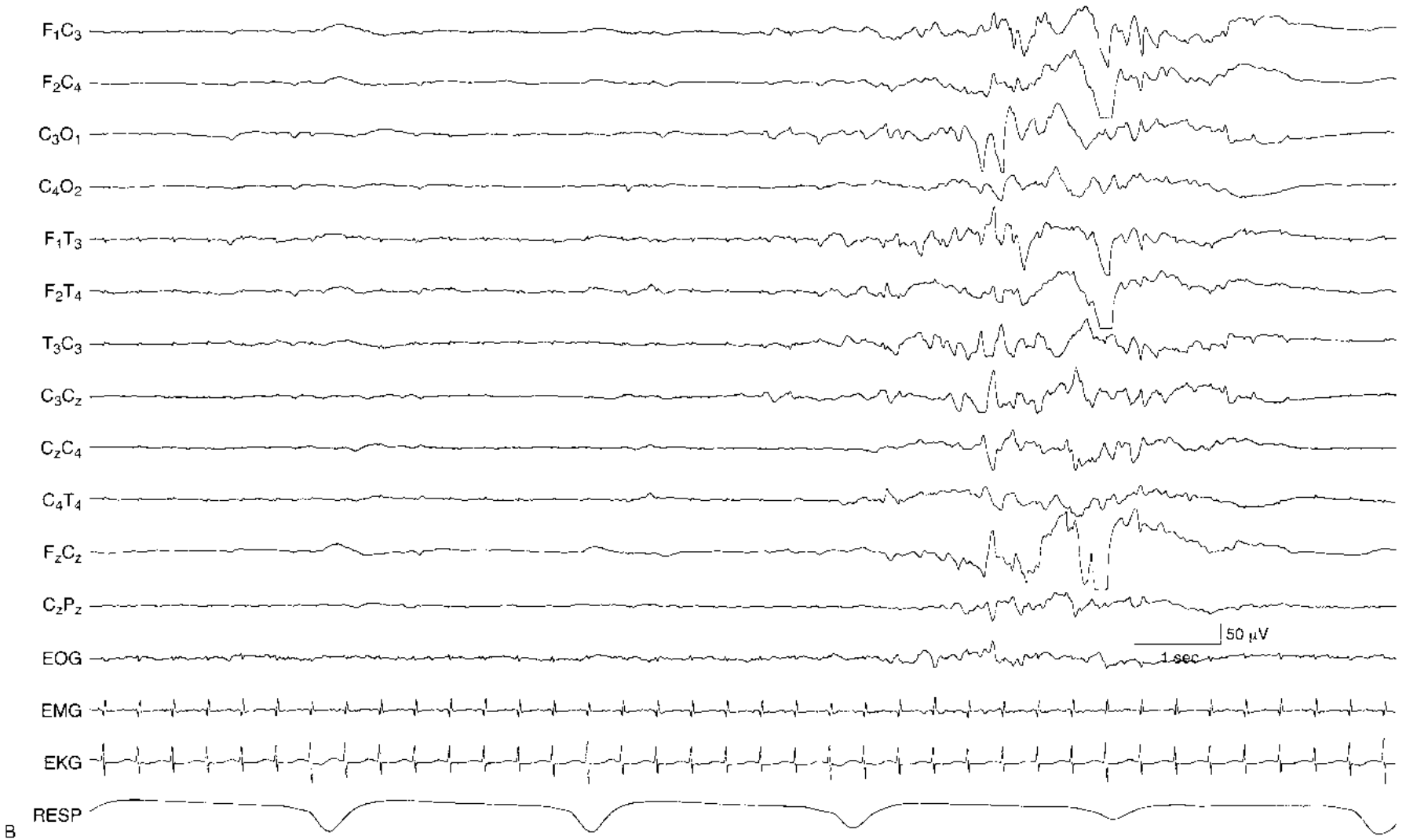


Figure 6.5 (*continued*)

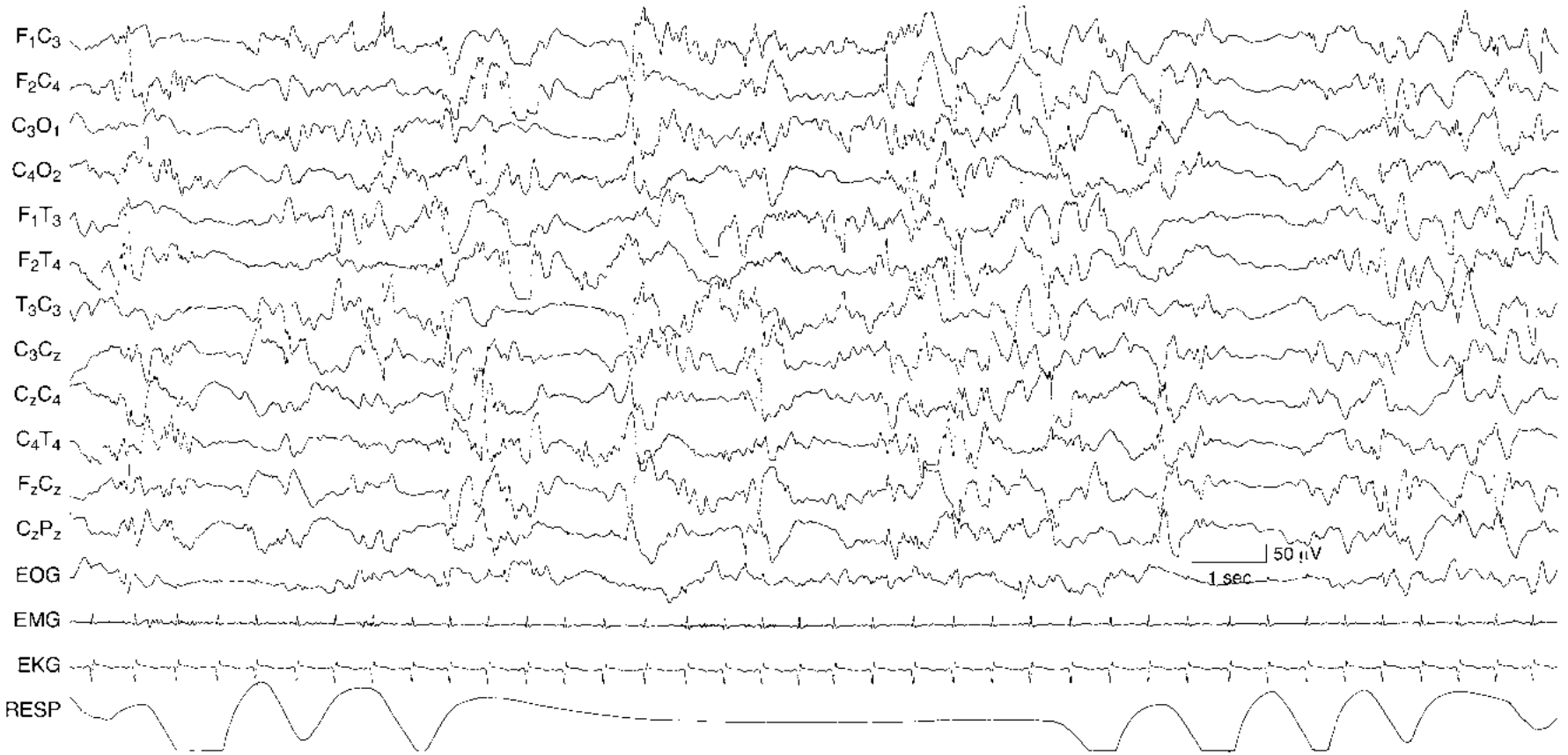


Figure 6.6 Generalized and regional episodes of voltage attenuation. There are brief episodes of generalized voltage attenuation lasting 1 to 2 sec and episodes of similar character and duration appearing independently in leads from the left and right hemispheres. The background activity is also abnormal with multifocal sharp waves. The EEG is from a 40-week CA infant who is lethargic and with CT neuroimaging findings of biparietal white matter lucencies. No specific etiology was identified.

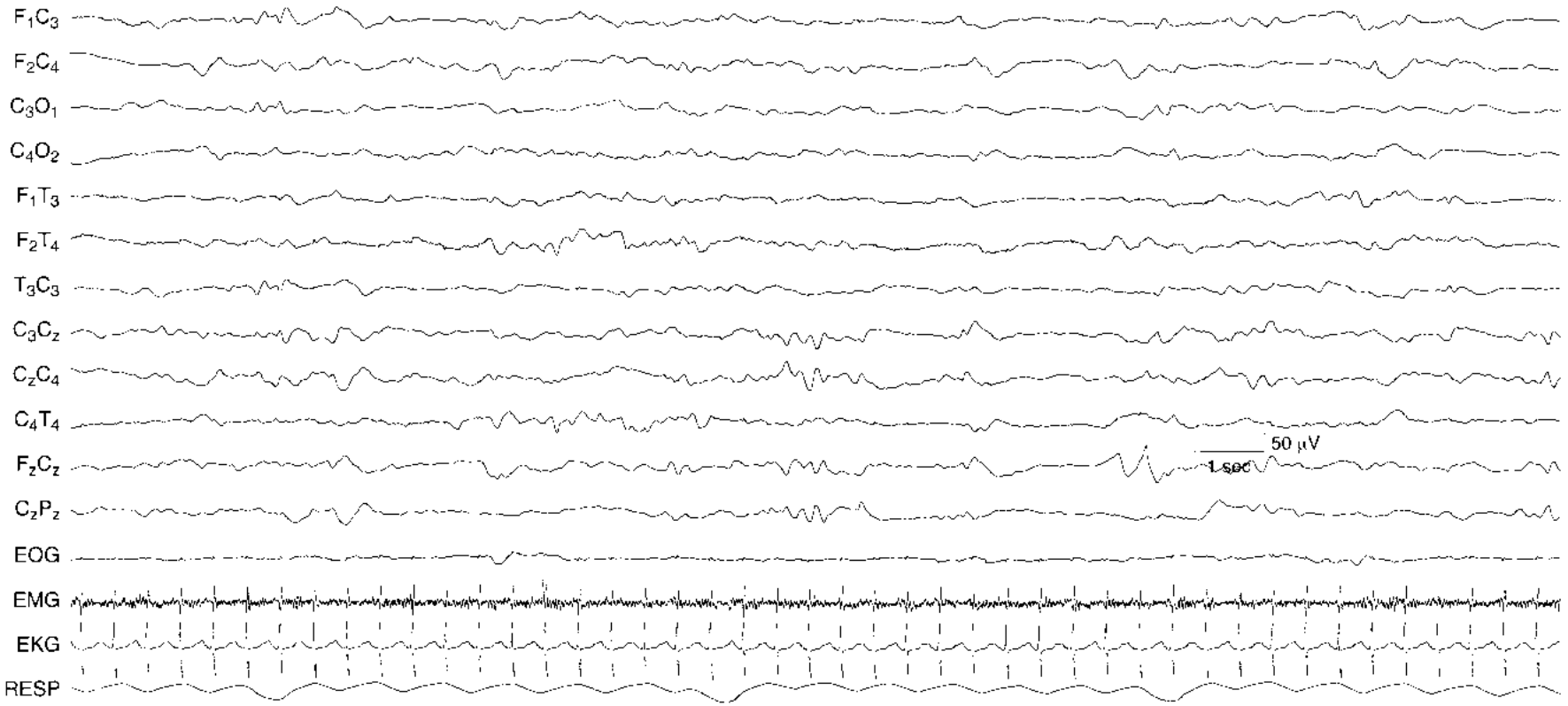


Figure 6.7 Undifferentiated background activity. The background EEG activity is undifferentiated. There is a lack of developmental milestones and a lack of activity of faster frequencies. The EEG is composed almost exclusively of moderate voltage slow activity. The infant is 43-week CA with the inborn error of metabolism, methylmalonic acidemia.

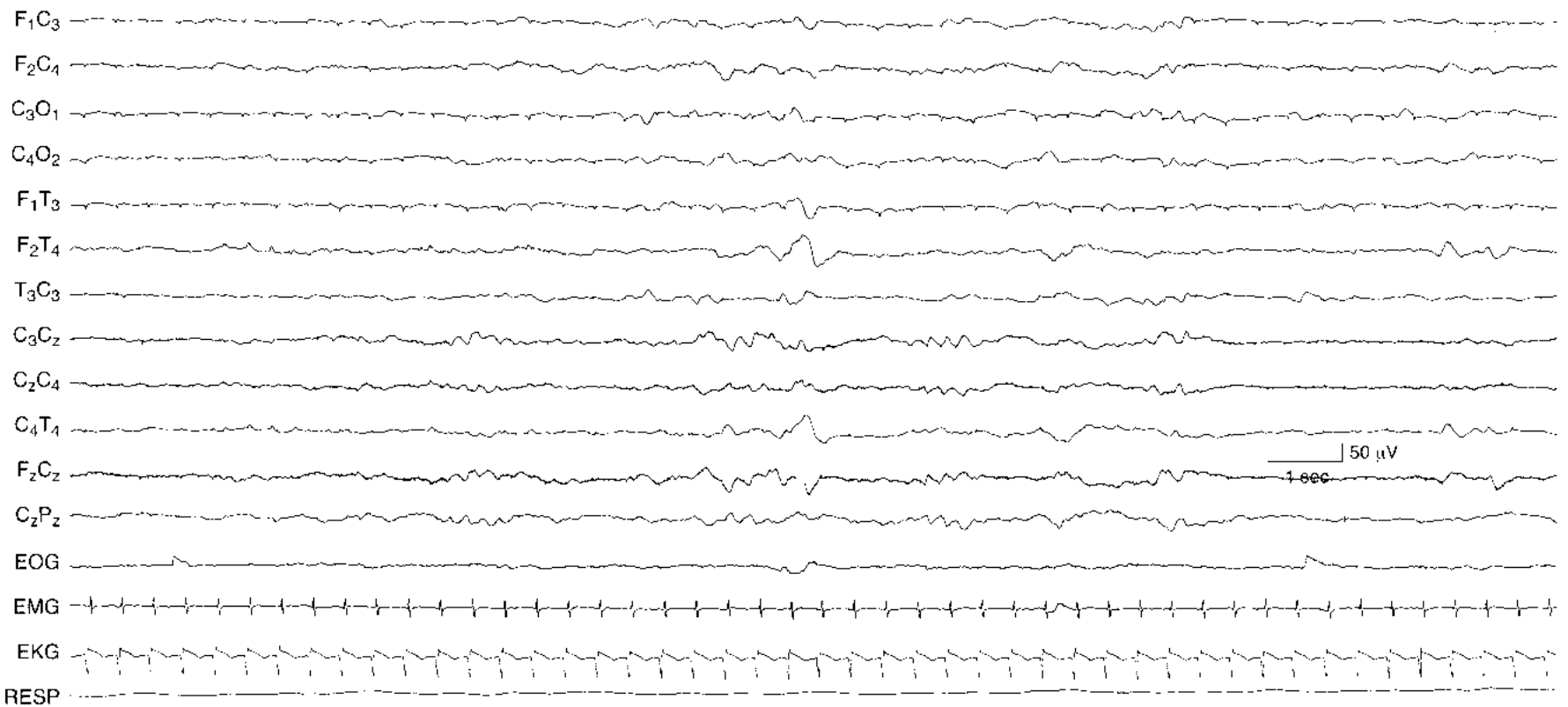


Figure 6.8 Undifferentiated background activity with periods of generalized voltage attenuation. The background activity is low in voltage and characterized by low- to moderate-voltage slow (theta and delta) activity with no alpha or beta activity. There are periods of generalized voltage attenuation early and late in the sample shown. The EEG is from a 41-week CA infant with renal failure and metabolic acidosis who was on renal dialysis at the time of recording.

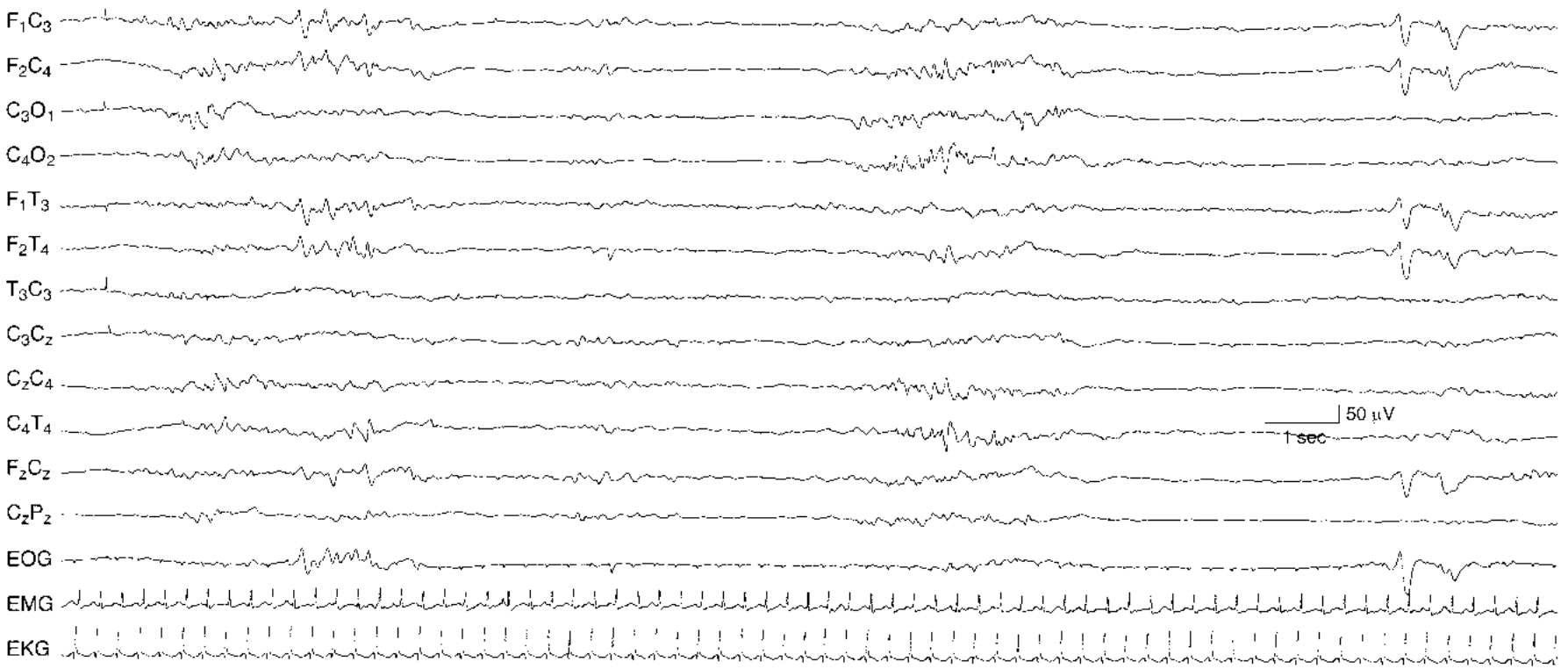


Figure 6.9 Undifferentiated background with episodes of generalized voltage attenuation, but with preservation of some developmental milestones. The background activity is undifferentiated. There is intermittent rhythmic theta activity that occurs between episodes of generalized voltage attenuation. Early in the sample, there are abnormal sharp waves in the frontal regions. However, later in the sample, normal frontal sharp transients are present. Such findings can be distinguished from a suppression-burst pattern when other portions of the EEG are continuous and by the presence of normal developmental milestones. The EEG is from a 39-week CA infant with congenital heart disease and chronic hypoxemia.

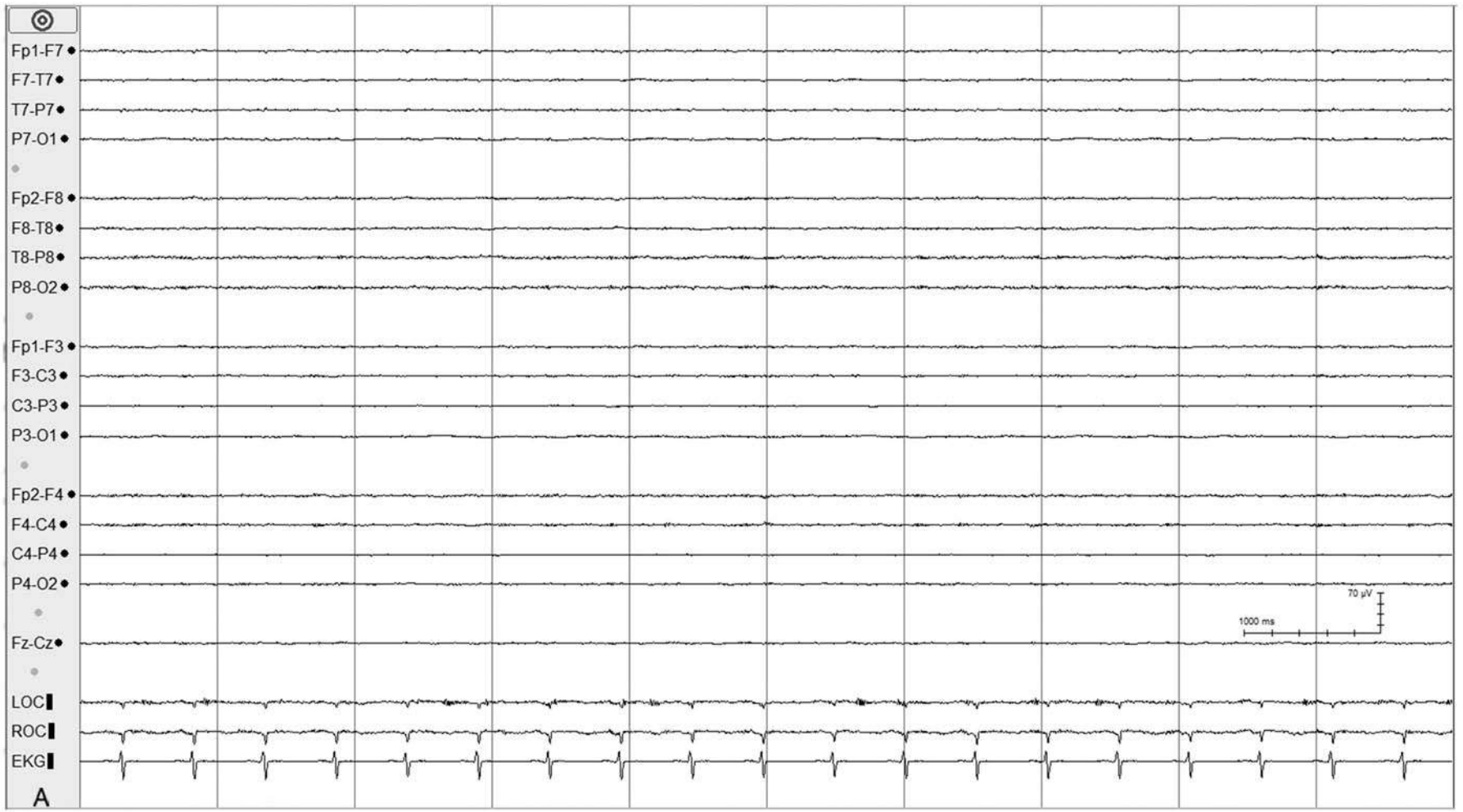


Figure 6.10 (A)–(C) Monitoring during hypothermia protocol. (A) Day 1 of hypothermia protocol (temperature 90.1°F, 32.3°C). The background activity is depressed and undifferentiated in the EEG of this 38-week CA infant with hypoxic ischemic encephalopathy. (*continued*)

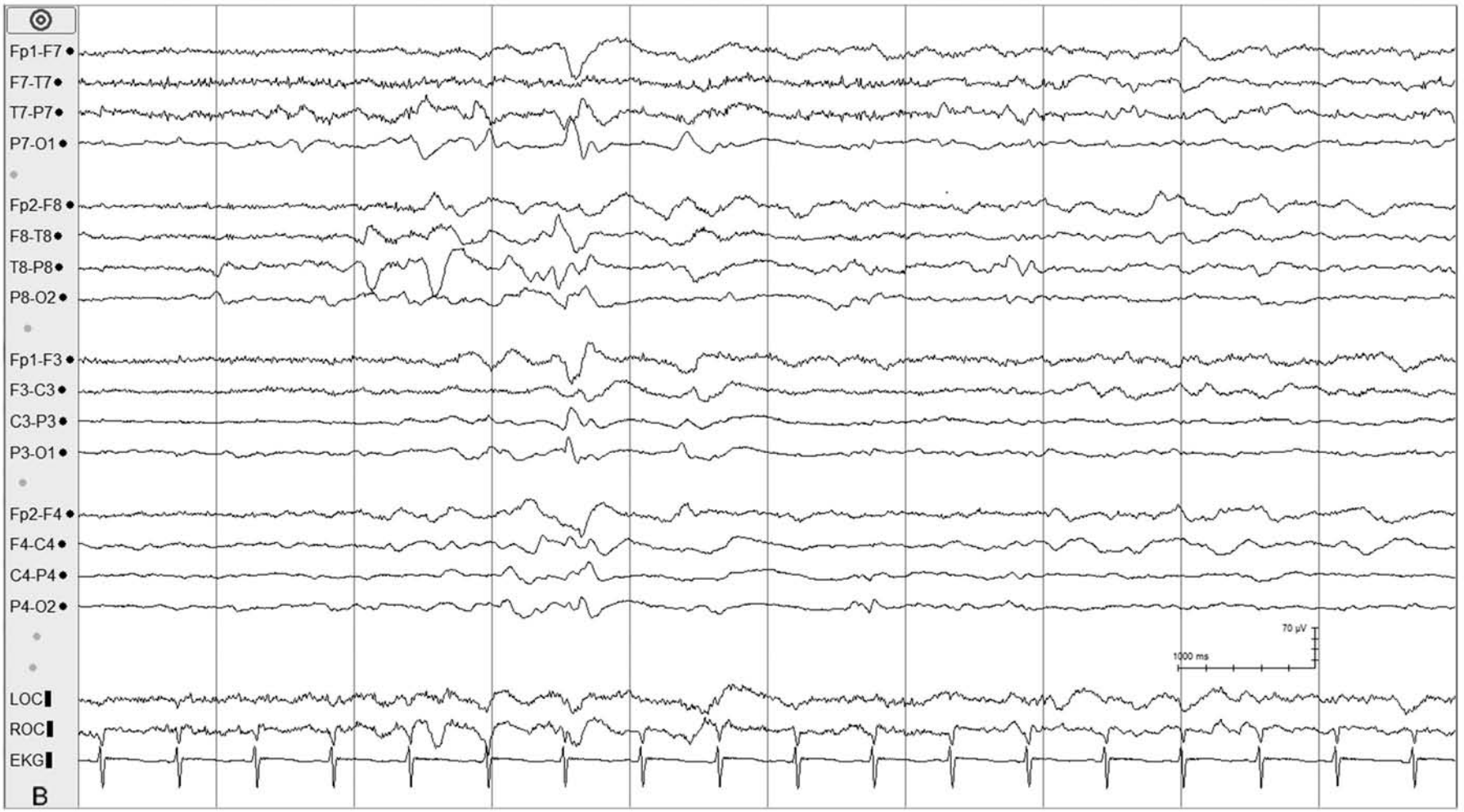


Figure 6.10 (*continued*) **(B)** Day 3 of hypothermia protocol; the background has evolved to relatively continuous activity with multifocal sharp waves. (*continued*)

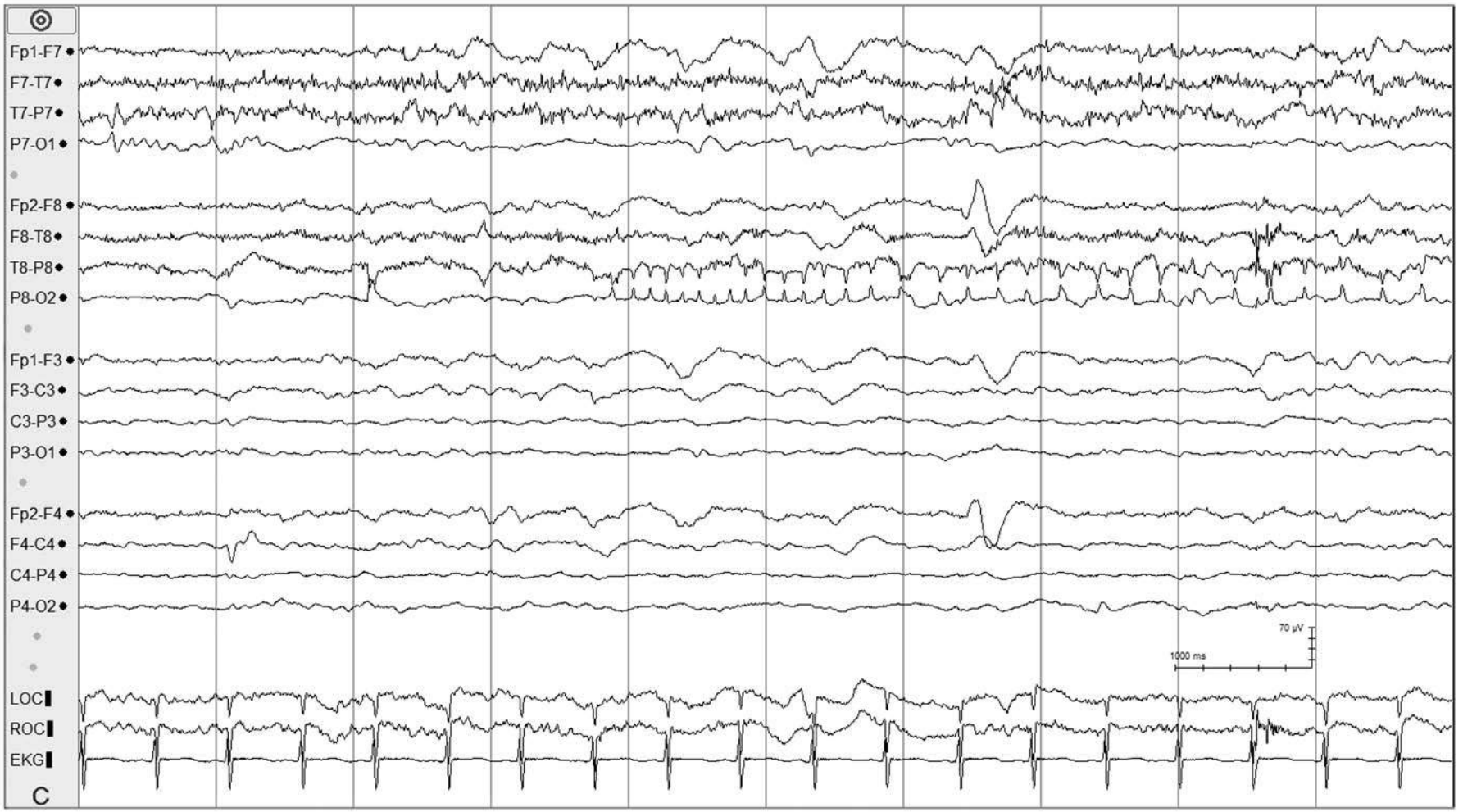


Figure 6.10 (*continued*) **(C)** Day 3 of hypothermia protocol; electrical seizure activity emerges in the right parietal region.

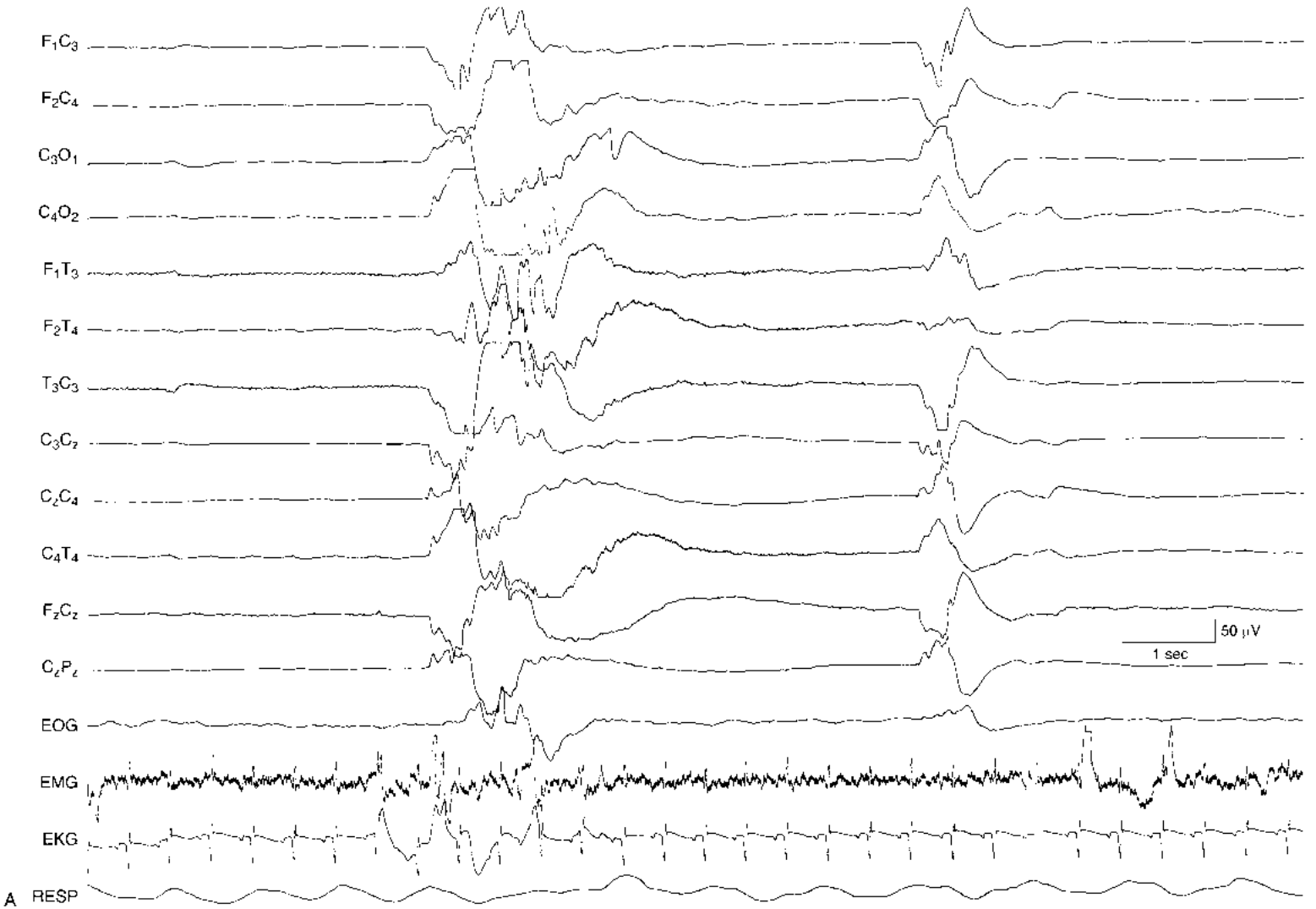
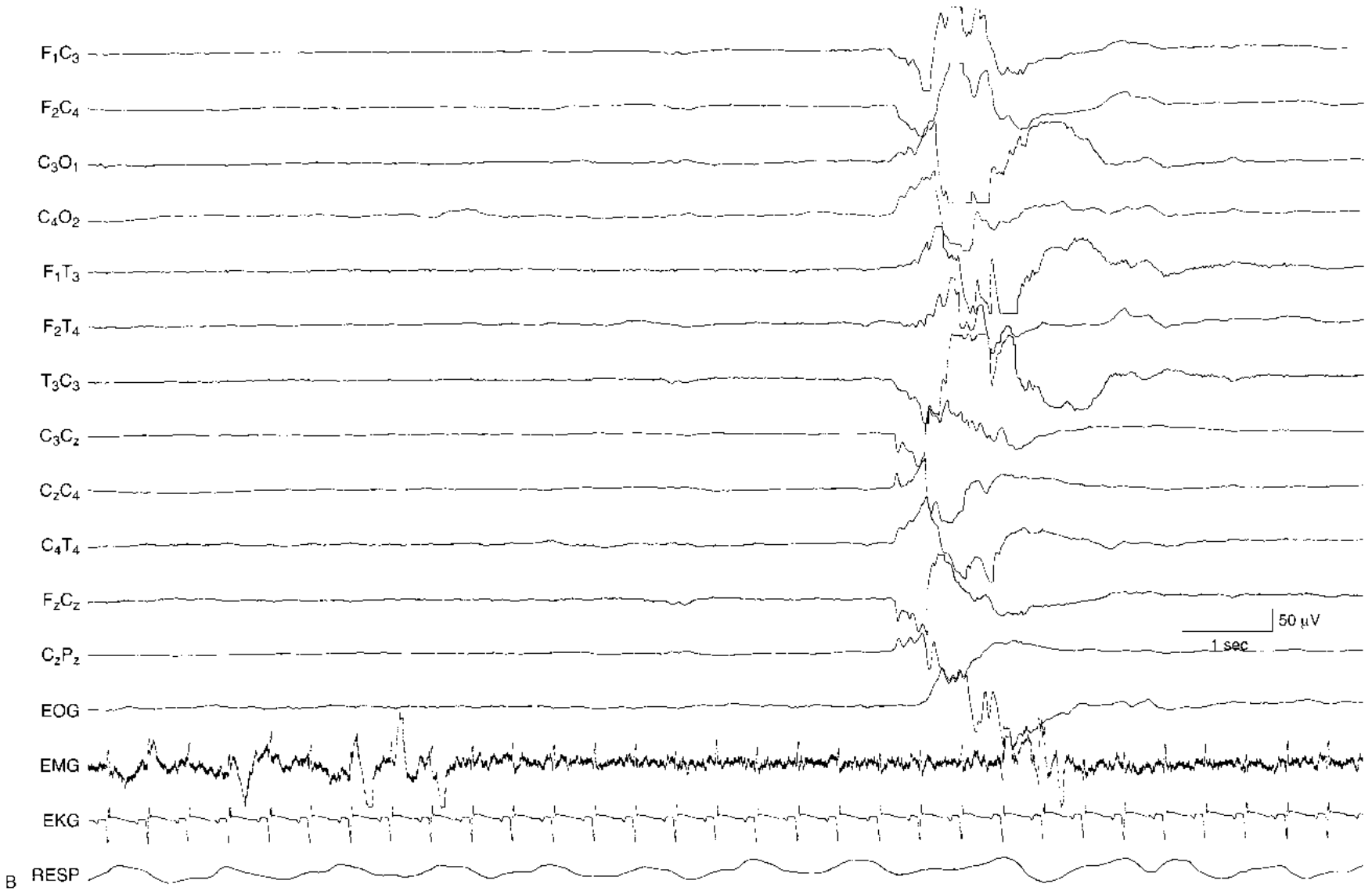


Figure 6.11 (A) and (B) Suppression-burst activity with sharp and slow waves within the bursts and variable durations between bursts. The brief bursts are characterized by high-voltage slow activity with superimposed theta and alpha activity. The bursts are followed by high-voltage very slow-wave transients. The periods of suppression are variable in these contiguous samples **(A)** and **(B)**, lasting from 3 sec to over 10 sec. This EEG was recorded from a 35-week CA infant who was lethargic with hypoxic-ischemic encephalopathy, microcephaly, and the finding of periventricular leukomalacia on head CT. (*continued*)



B

Figure 6.11 (*continued*)

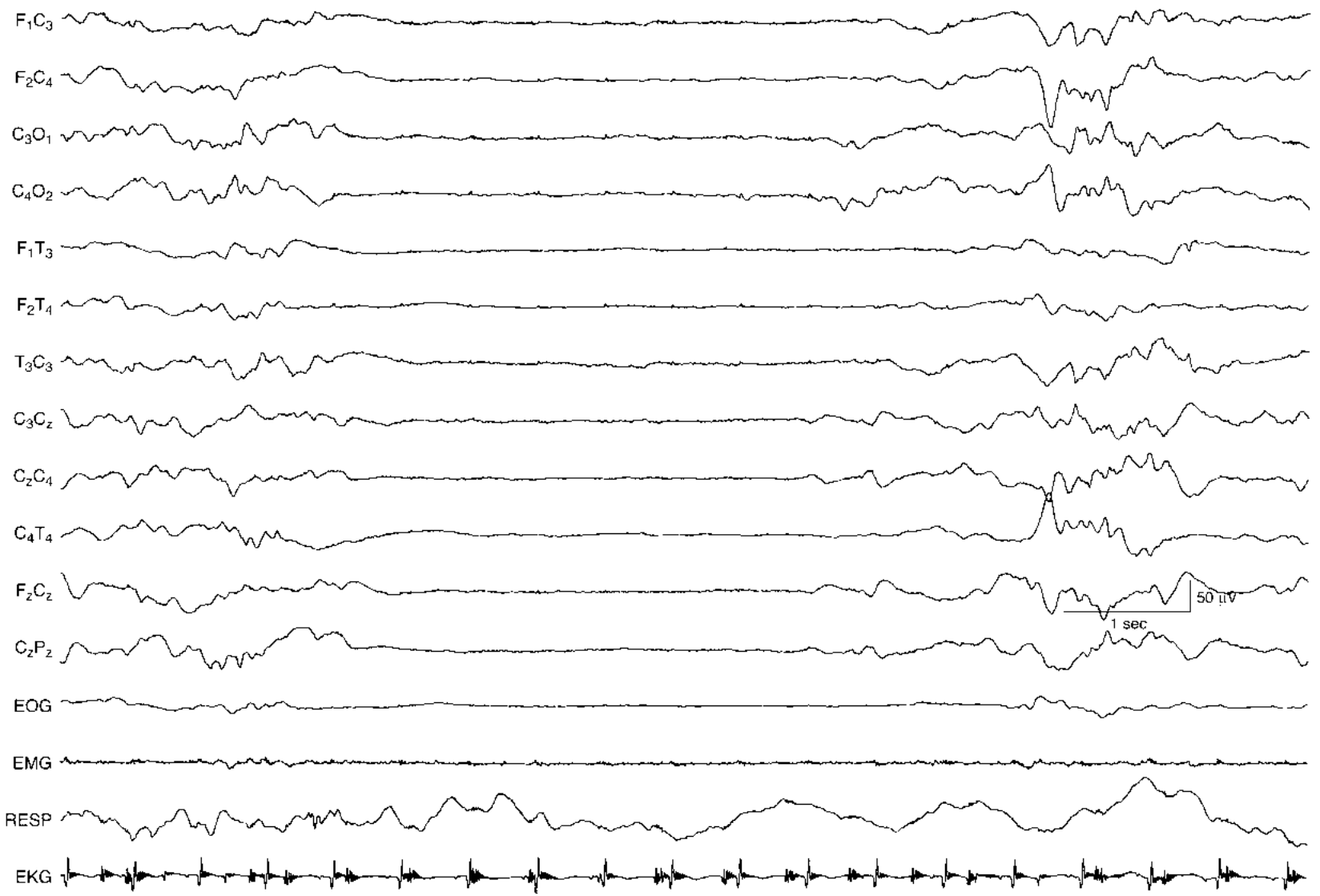


Figure 6.12 Suppression-burst activity with activity of normal character within the bursts. The bursts are characterized by moderate-voltage activity of mixed slow and faster frequencies, that if continuous, would be considered normal for this full-term infant. However, the background activity is suppression burst. This term infant suffered meconium aspiration, required ventilatory support, and, by the time of this recording, was maintained with ECMO.

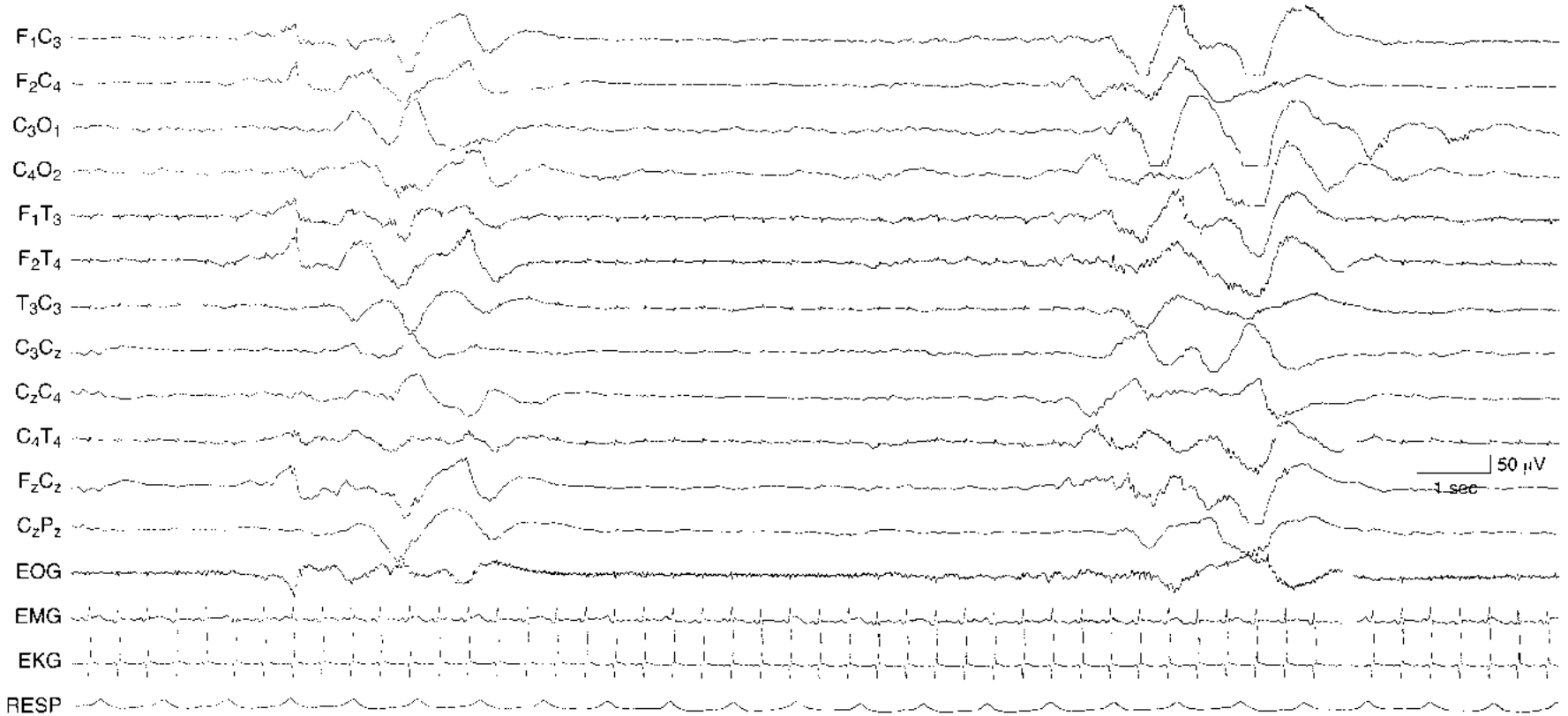


Figure 6.13 Suppression-burst activity with bursts of asynchronous, very slow, and superimposed fast activity. The bursts are characterized by high voltage, very slow activity with superimposed low voltage faster activity. This occurs asynchronously on the two sides. The infant is 37-weeks CA, with hypoxic-ischemic encephalopathy, multisystem organ failure, and intracerebral hemorrhage on the left—in this instance with no consistent lateralizing findings on EEG.

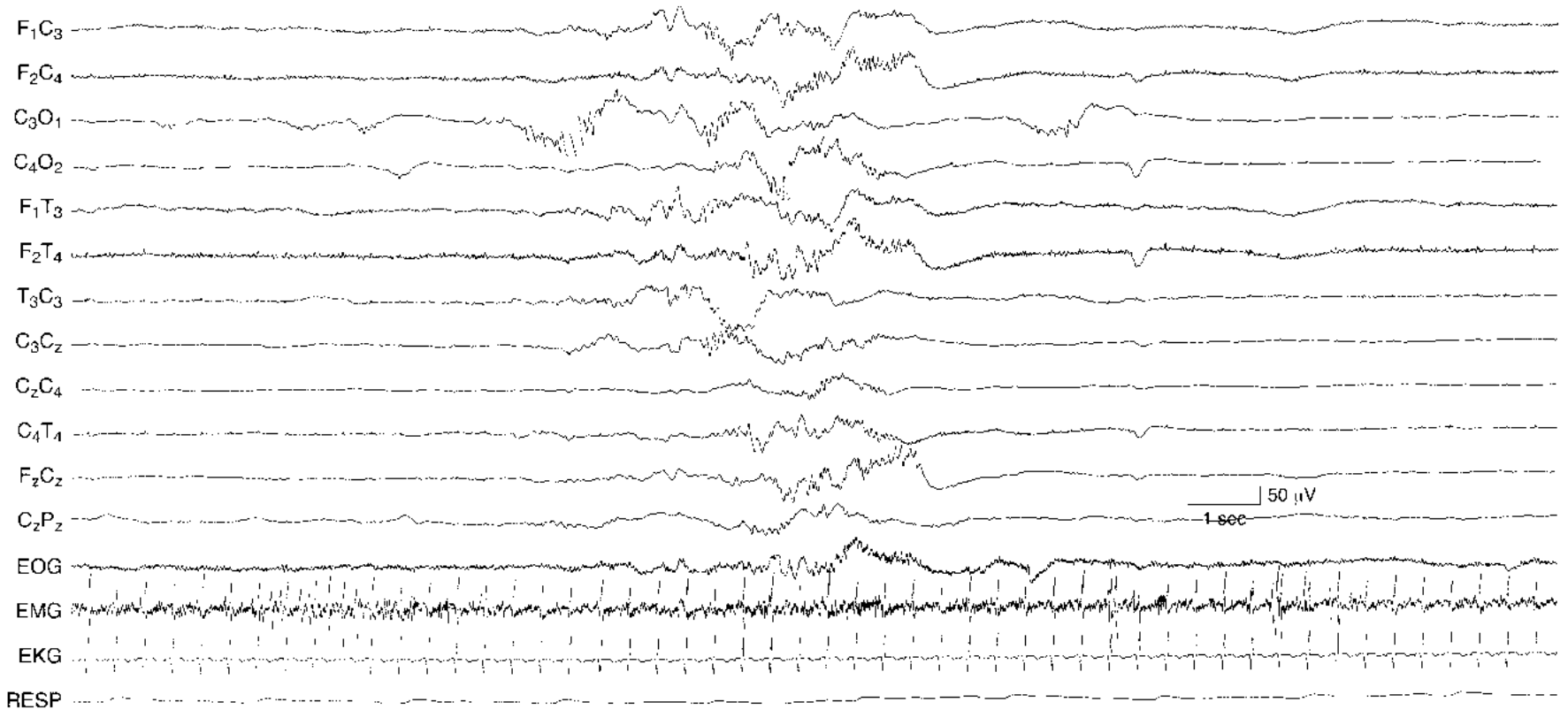


Figure 6.14 Suppression-burst activity with predominance of fast activity within the bursts. Runs of moderate-voltage fast activity are present asynchronously on the two sides during periods of bursting. The infant is 35-weeks CA with metabolic acidosis, cardiac failure, pulmonary edema, peritonitis, and microcephaly.

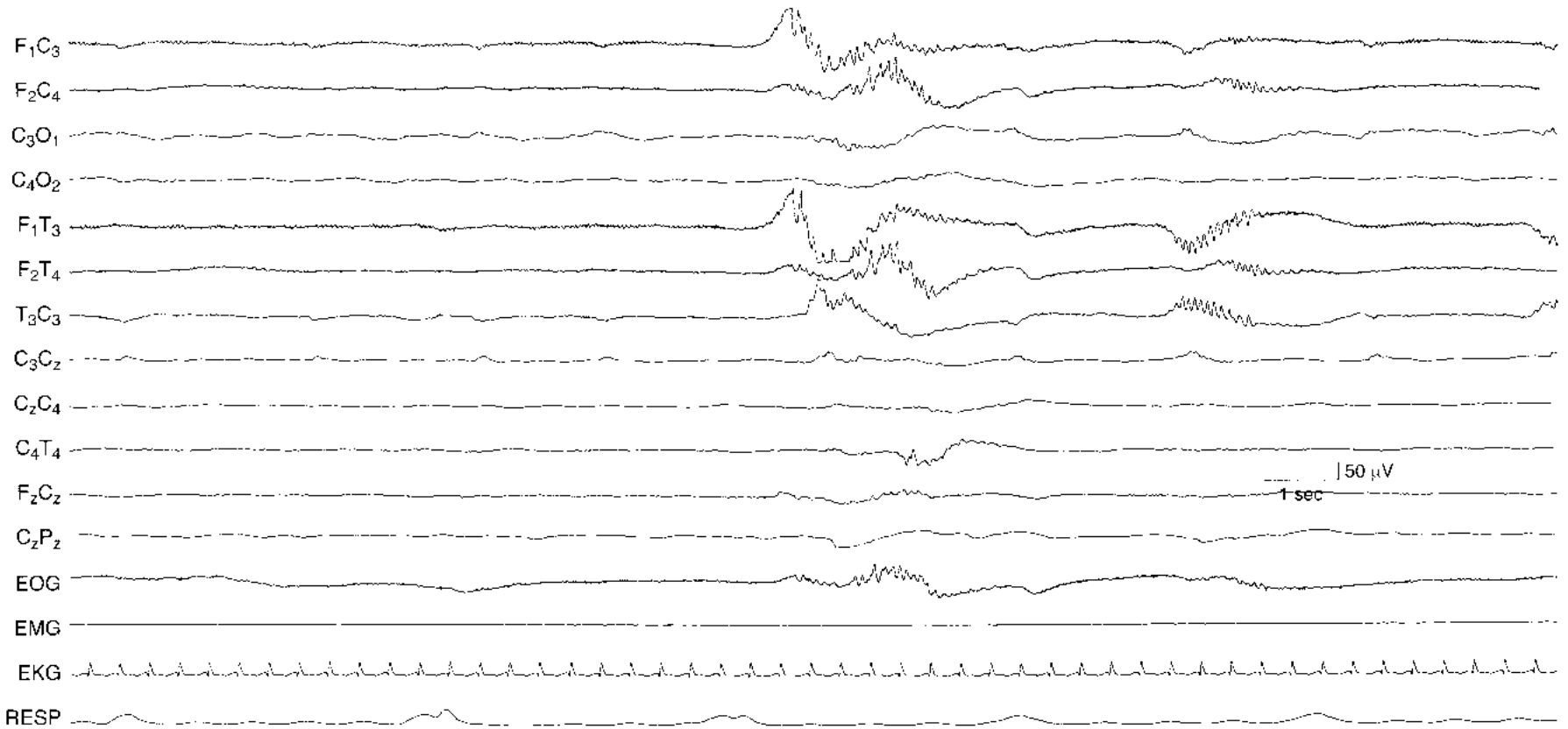


Figure 6.15 Suppression-burst activity with rhythmic alpha activity within the bursts. There are runs of moderate-voltage rhythmic alpha activity in the frontal temporal regions that appear asynchronously within the bursts of this suppression-burst recording. This EEG is from a 35-week CA infant with hypoxic-ischemic encephalopathy.

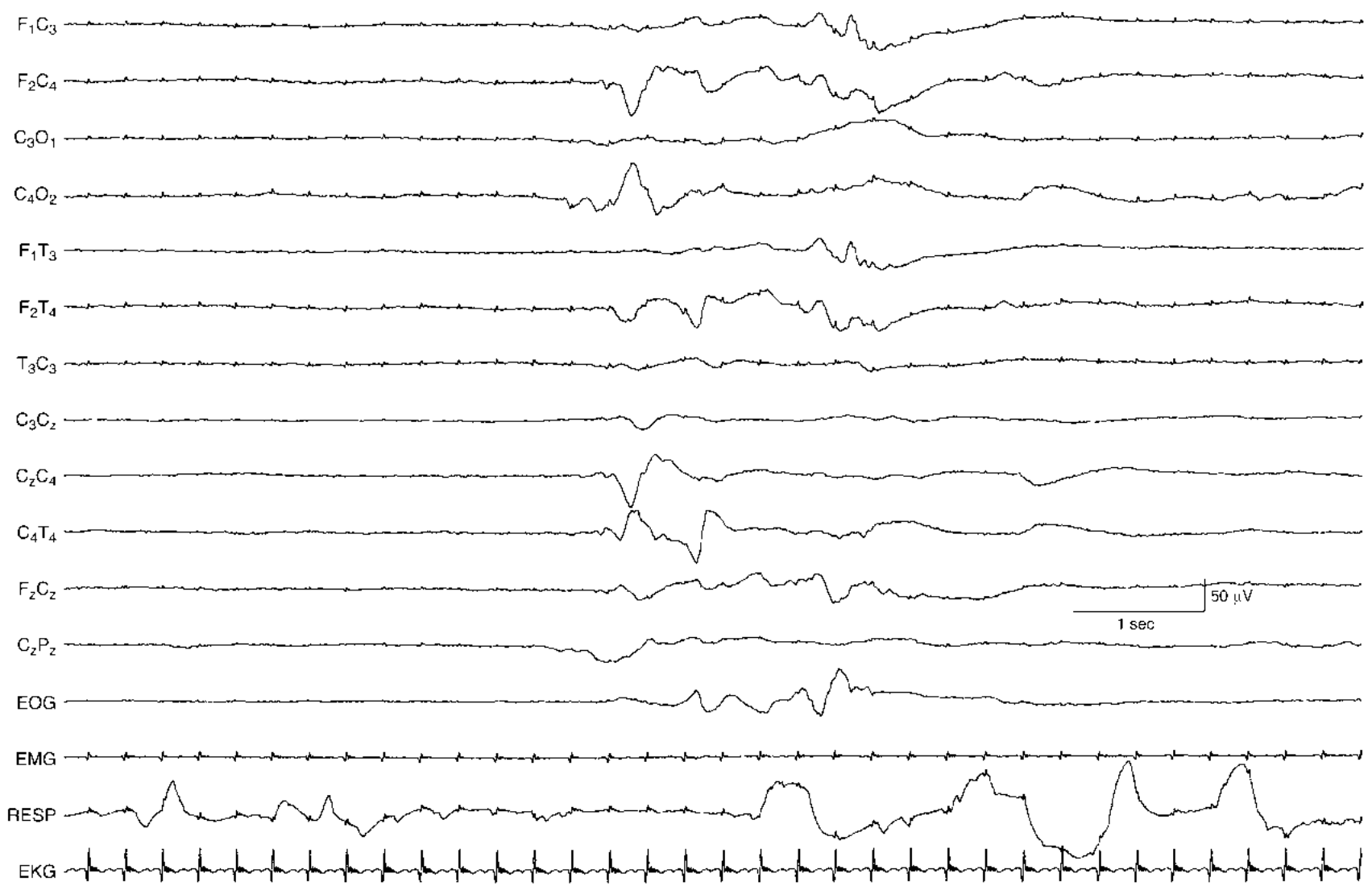


Figure 6.16 Suppression-burst activity with persistent asymmetry of activity within the bursts. The bursts are characterized by moderate-voltage theta and delta activity. There is a persistent voltage asymmetry of the bursts with the amplitudes of waves lower in leads from the left central-temporal region compared to homologous regions on the right. This term infant was born by emergency cesarean section and had persistent cyanosis requiring support by ECMO. The asymmetry on EEG is most likely due to dependent scalp edema on the left.

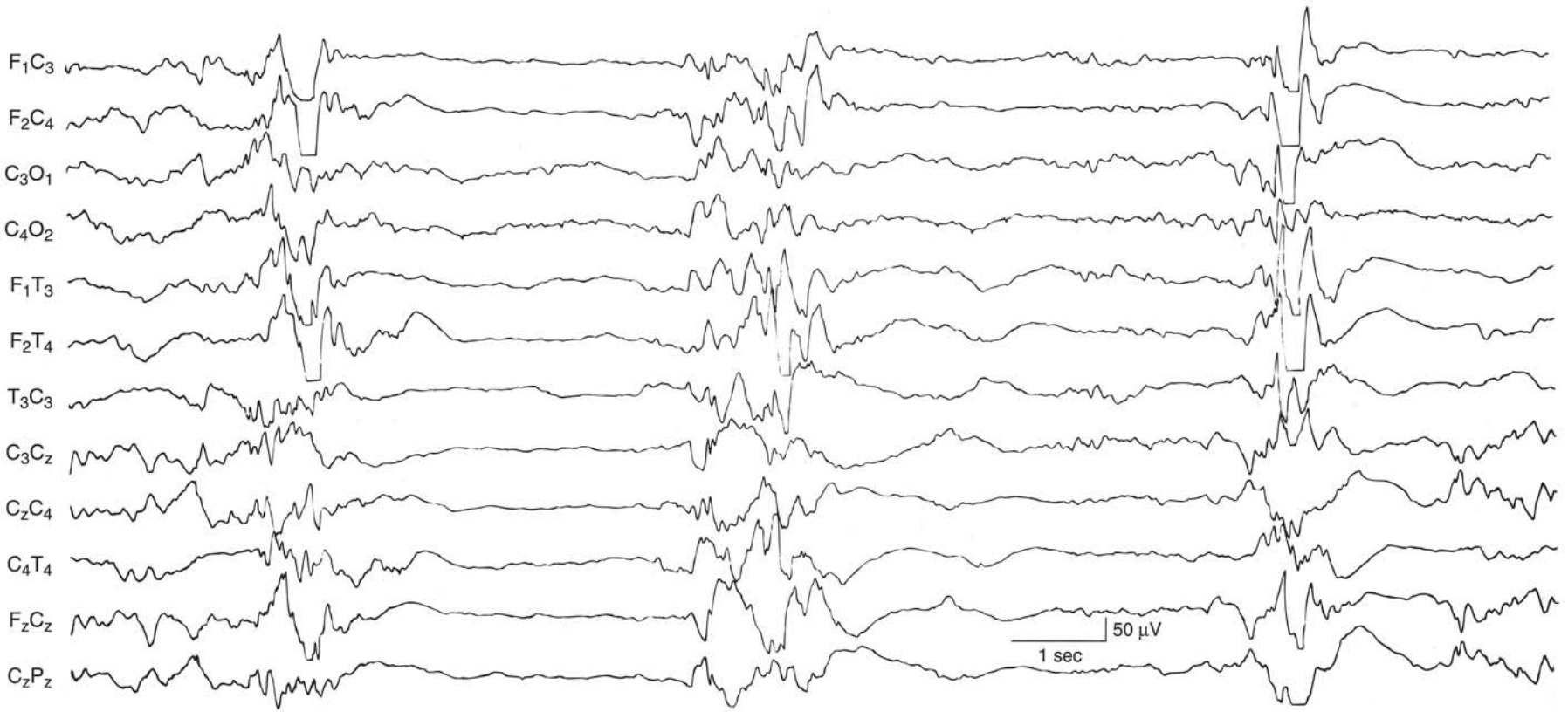


Figure 6.17 Suppression-burst activity with synchronous bursts associated with myoclonus. The bursts recur periodically every 3 to 5 sec, but are brief, lasting 1 to 2 sec with fairly synchronous activity on the two sides. This term infant experienced generalized myoclonic and focal clonic seizures with the eventual finding of the inborn error of metabolism, nonketotic hyperglycinemia. (Mizrahi and Kellaway, 1998, with permission.)

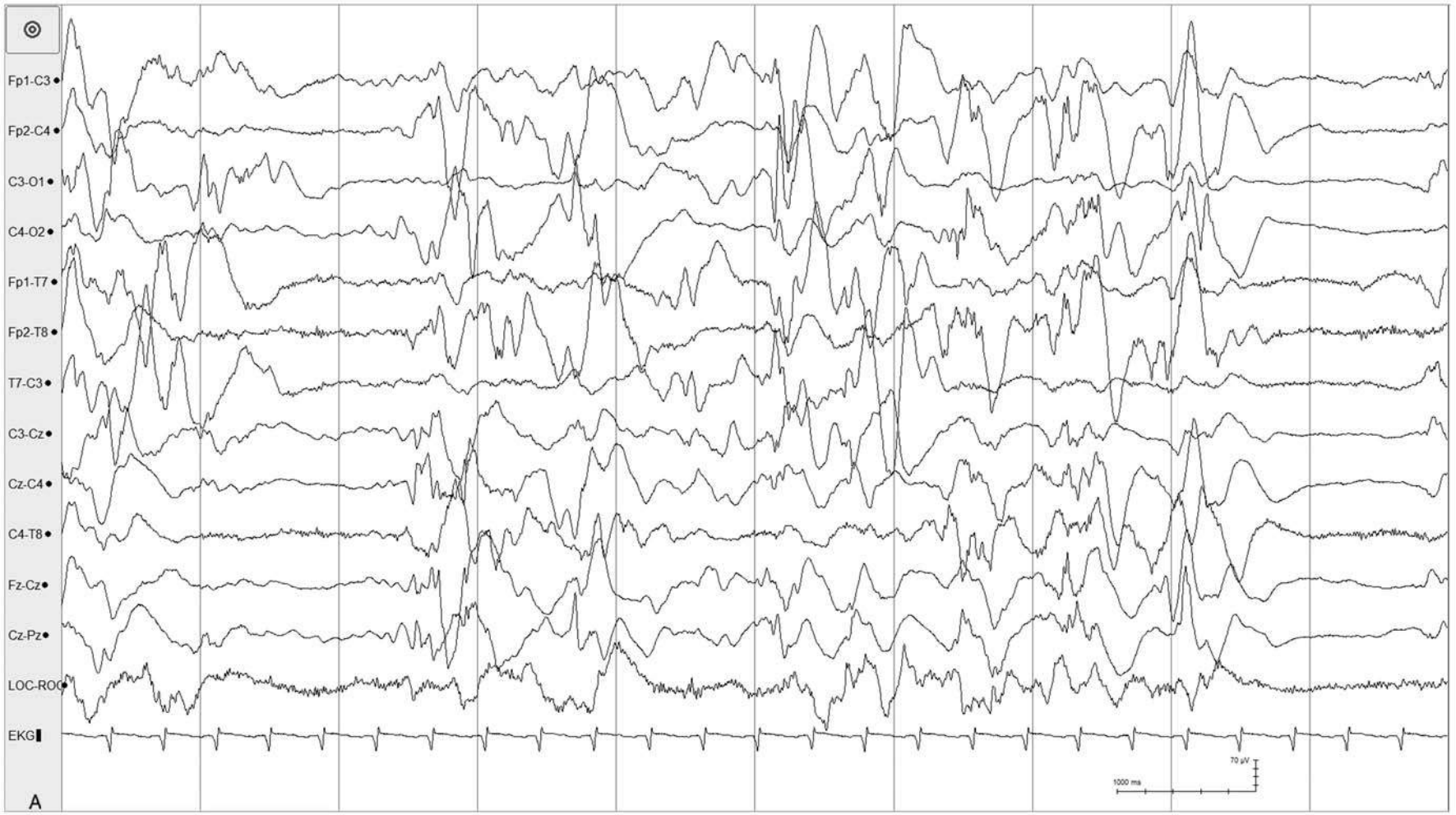


Figure 6.18 (A) and (B) Asynchronous suppression-burst pattern. (A) Suppression-burst pattern is present independently in the left and right hemispheres in this 40-week CA, 27-day infant with early infantile epileptic encephalopathy associated with an ARX mutation. (*continued)*

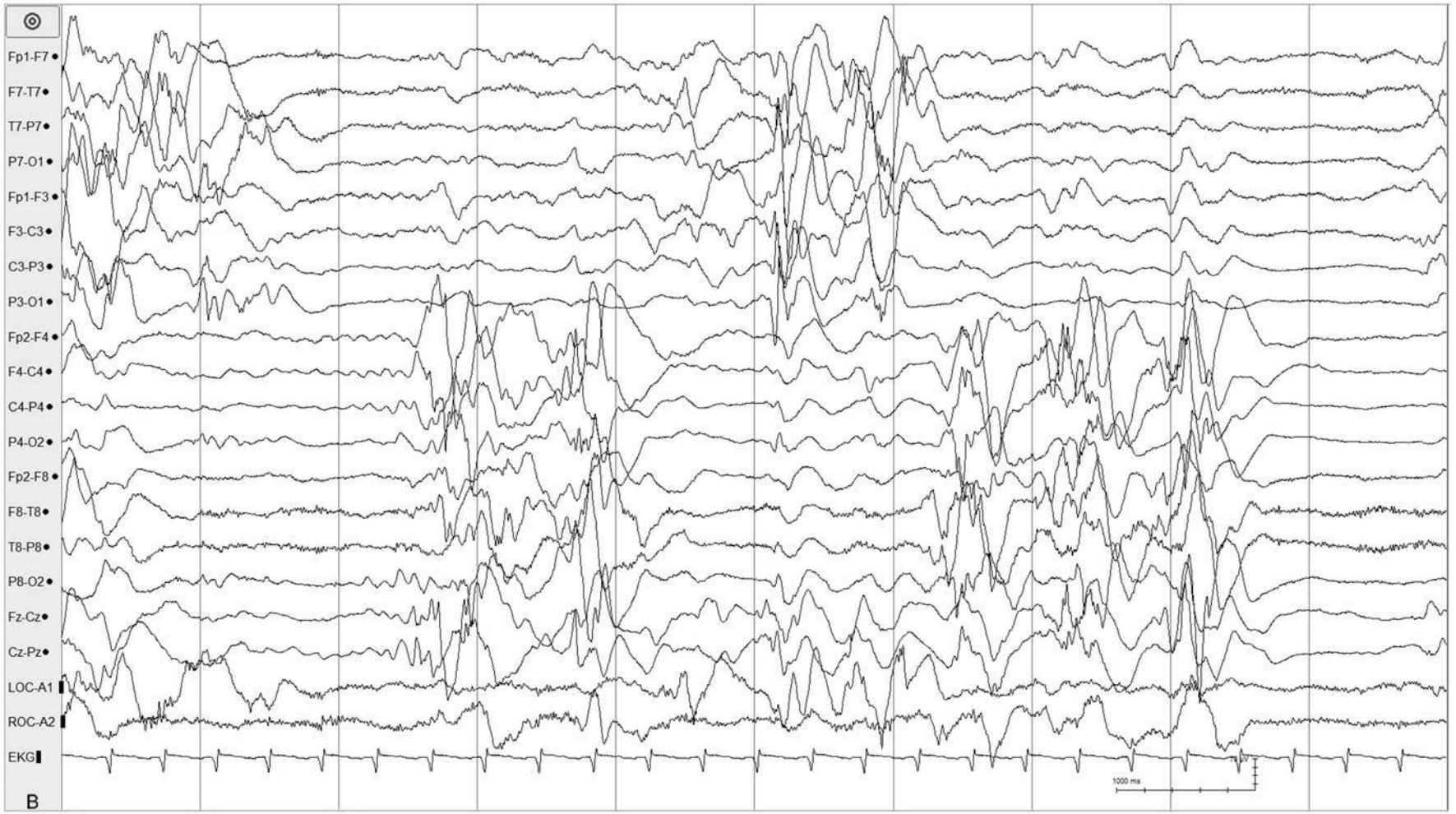


Figure 6.18 (*continued*) **(B)** The same sample shown in **(A)** is remontaged to more clearly demonstrate the asynchrony of the suppression-burst pattern.

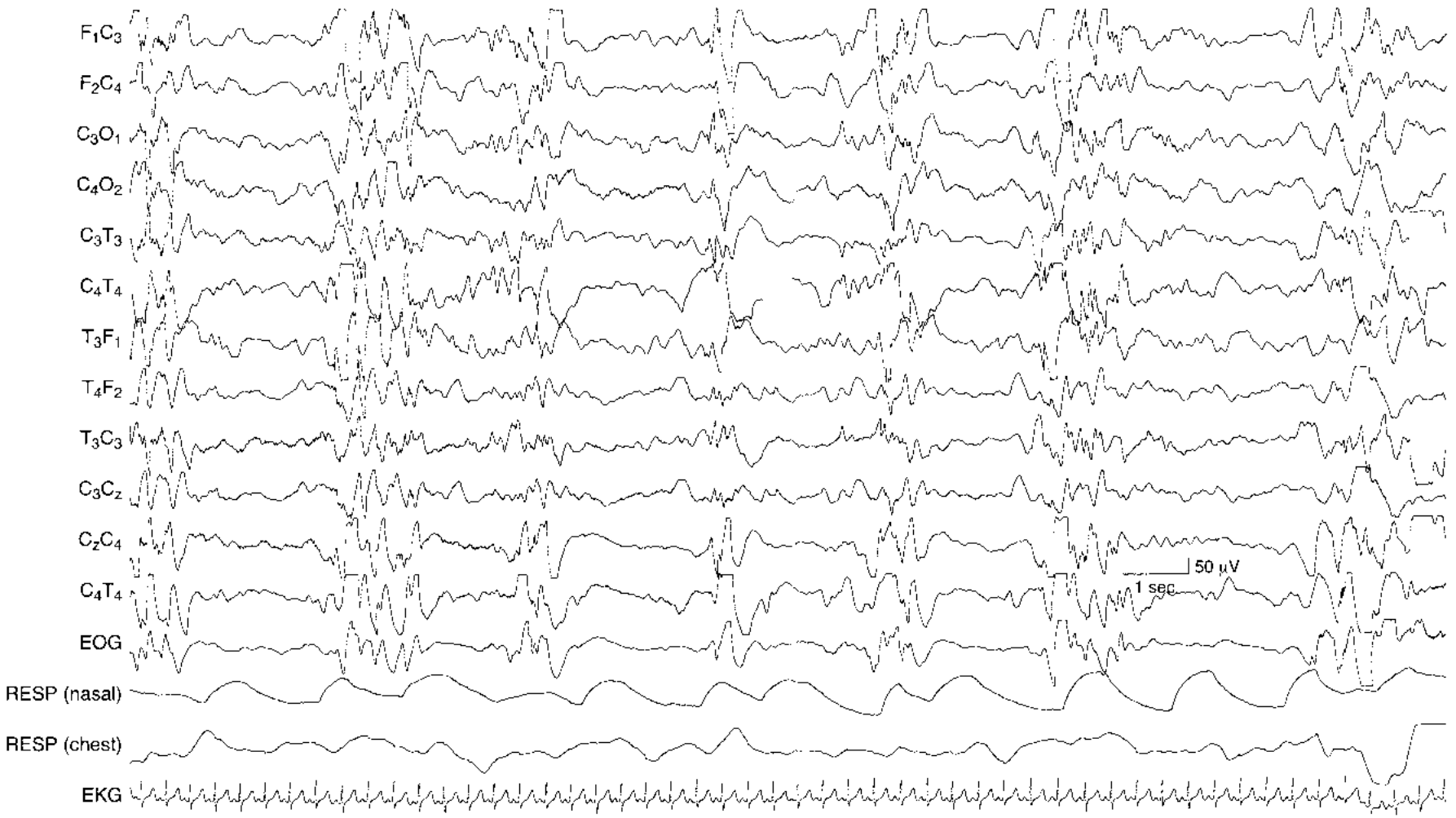


Figure 6.19 Suppression burst with multifocal, high-voltage spikes. This is a suppression-burst variant of hypsarrhythmia in a 43-week CA infant with an inborn error of metabolism and a clinical diagnosis of early myoclonic encephalopathy. The infant experienced infantile spasms that were accompanied by generalized voltage attenuations in the EEG (not shown).

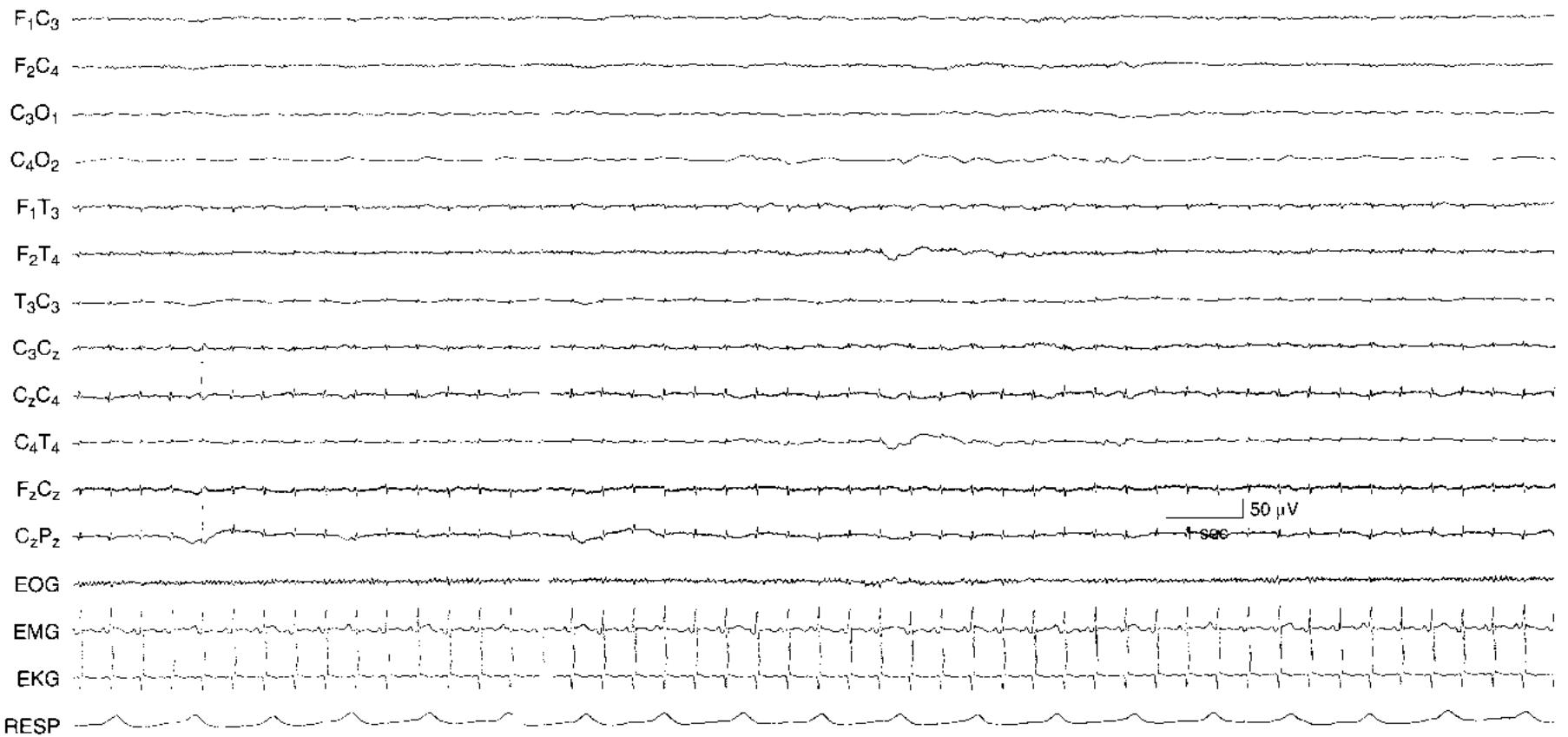


Figure 6.20 Depressed and undifferentiated background activity. The background activity is severely depressed and undifferentiated in all regions with only ECG artifact and occasional very low voltage slow waves present. This EEG is from a 37-week CA infant with hypoxic-ischemic encephalopathy (APGAR scores 1 at 1 minute, 1 at 5 minute), multiorgan systems failure, and intracerebral hemorrhage.

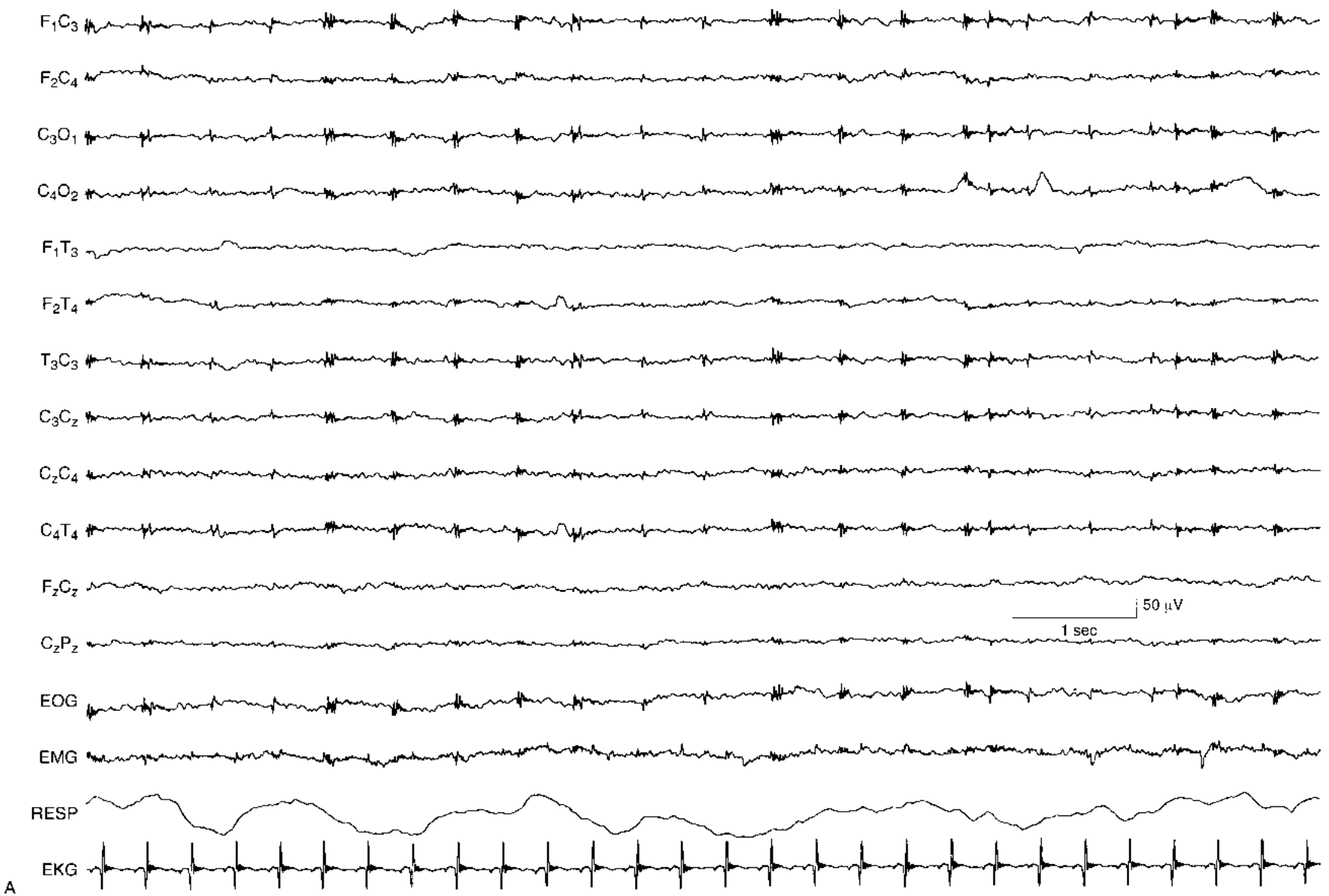


Figure 6.21 (A) and (B) Depressed and undifferentiated background activity (A) evolving to suppression-burst activity (B). (A) The EEG is depressed and undifferentiated with artifact from ECG and ECMO instrumentation. This EEG was recorded on Day 3 of life from this term infant with hypoxic-ischemic encephalopathy. (*continued*)

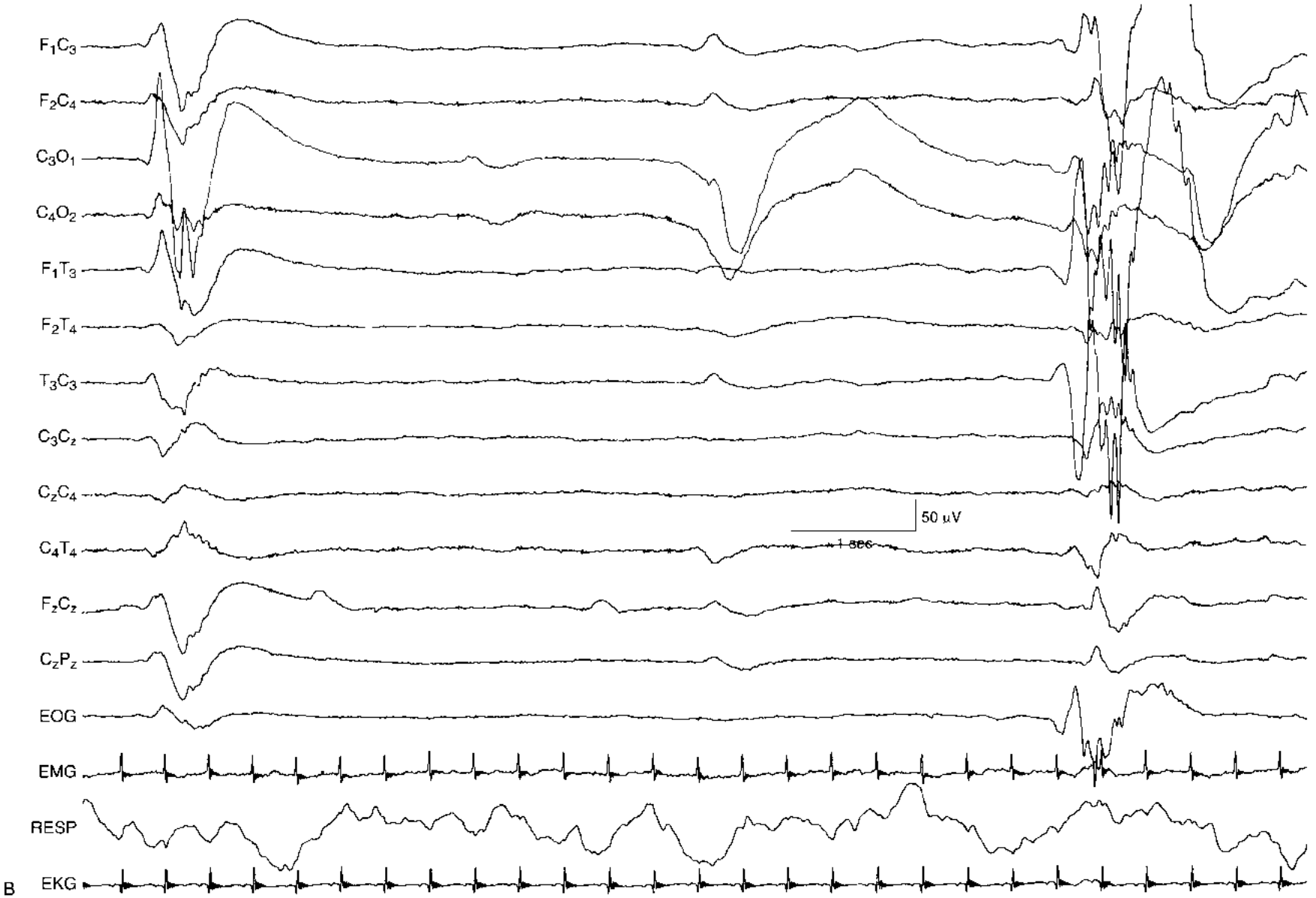


Figure 6.21 (*continued*) **(B)** On Day 10 of life, the EEG had evolved to a suppression-burst pattern. Although this represented a change in the EEG findings with some improvement, the rate of improvement and the change to only suppression burst suggest a poor prognosis in terms of neurological outcome.

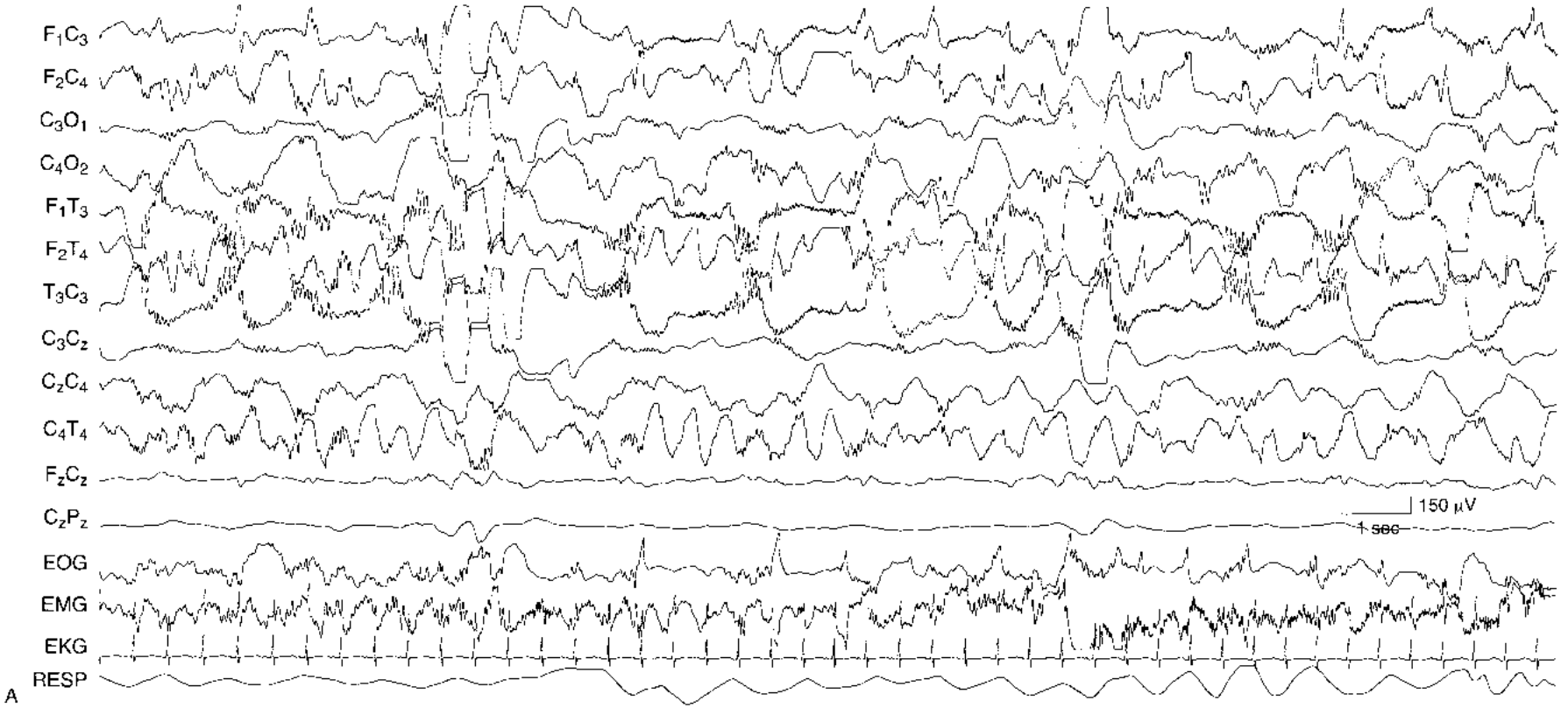


Figure 6.22 (A)–(C) Dynamic pattern of holoprosencephaly. These are samples from a single EEG recorded from a term infant with holoprosencephaly diagnosed by clinical and MRI findings. **(A)** There are multiple foci of spike and polyspike activity mixed with slow-wave activity. There is also independent delta activity with superimposed beta activity. (*continued*)

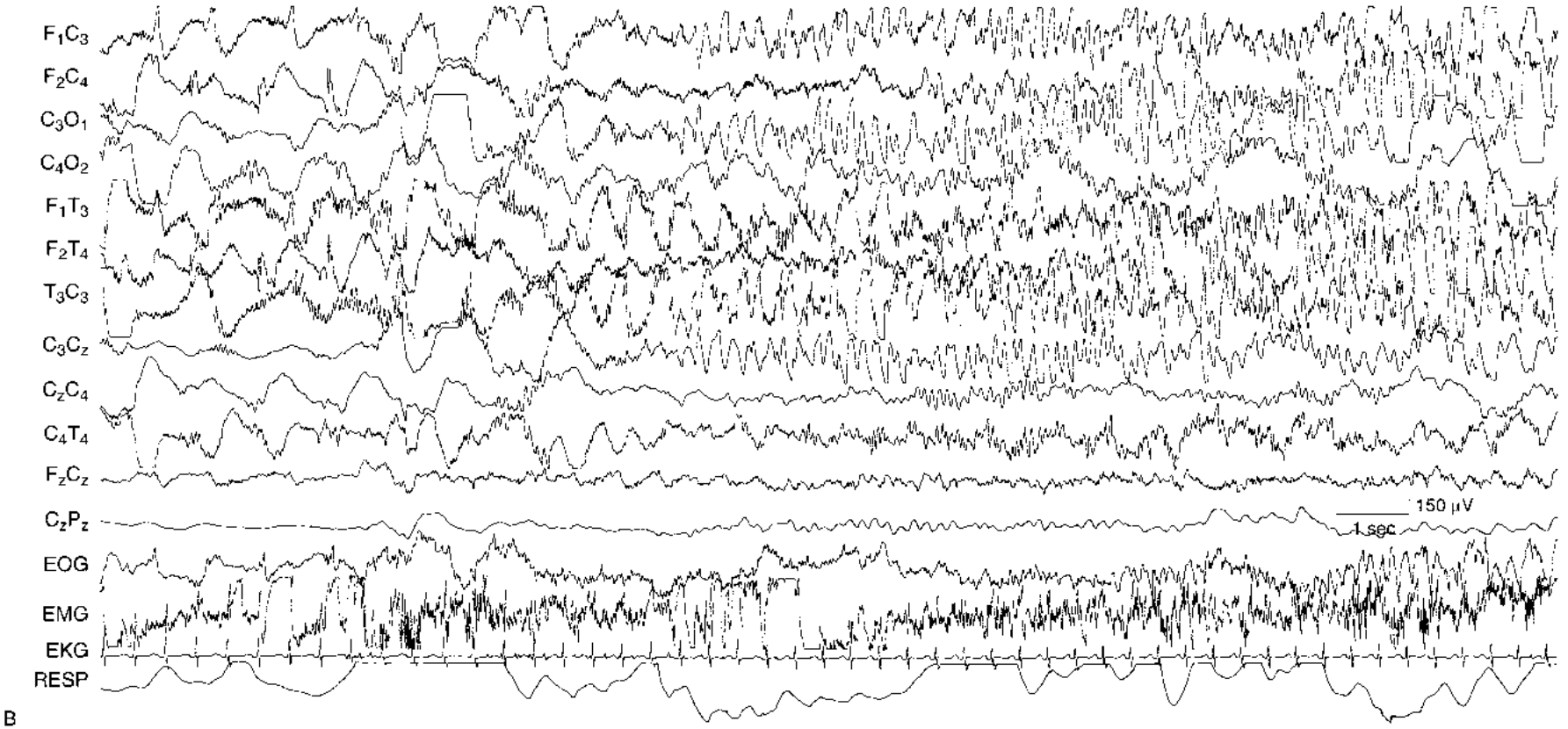


Figure 6.22 (*continued*) **(B)** There is a sudden transition to sustained rhythmic theta and alpha activity. (*continued*)

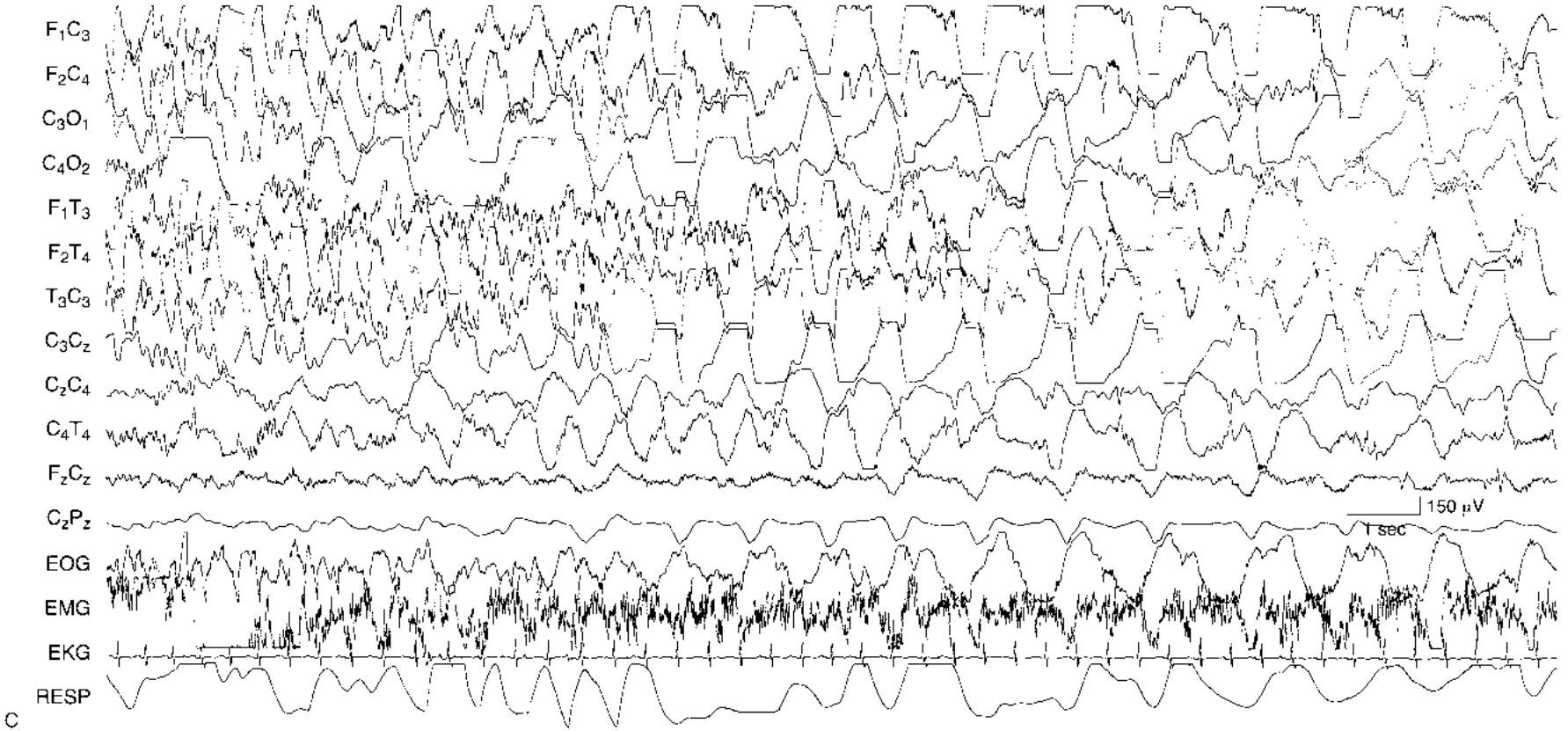


Figure 6.22 (*continued*) **(C)** There is a sudden transition to high-voltage rhythmic slow activity predominantly on the left. Note the voltage calibration that indicates the very high voltage of this activity.

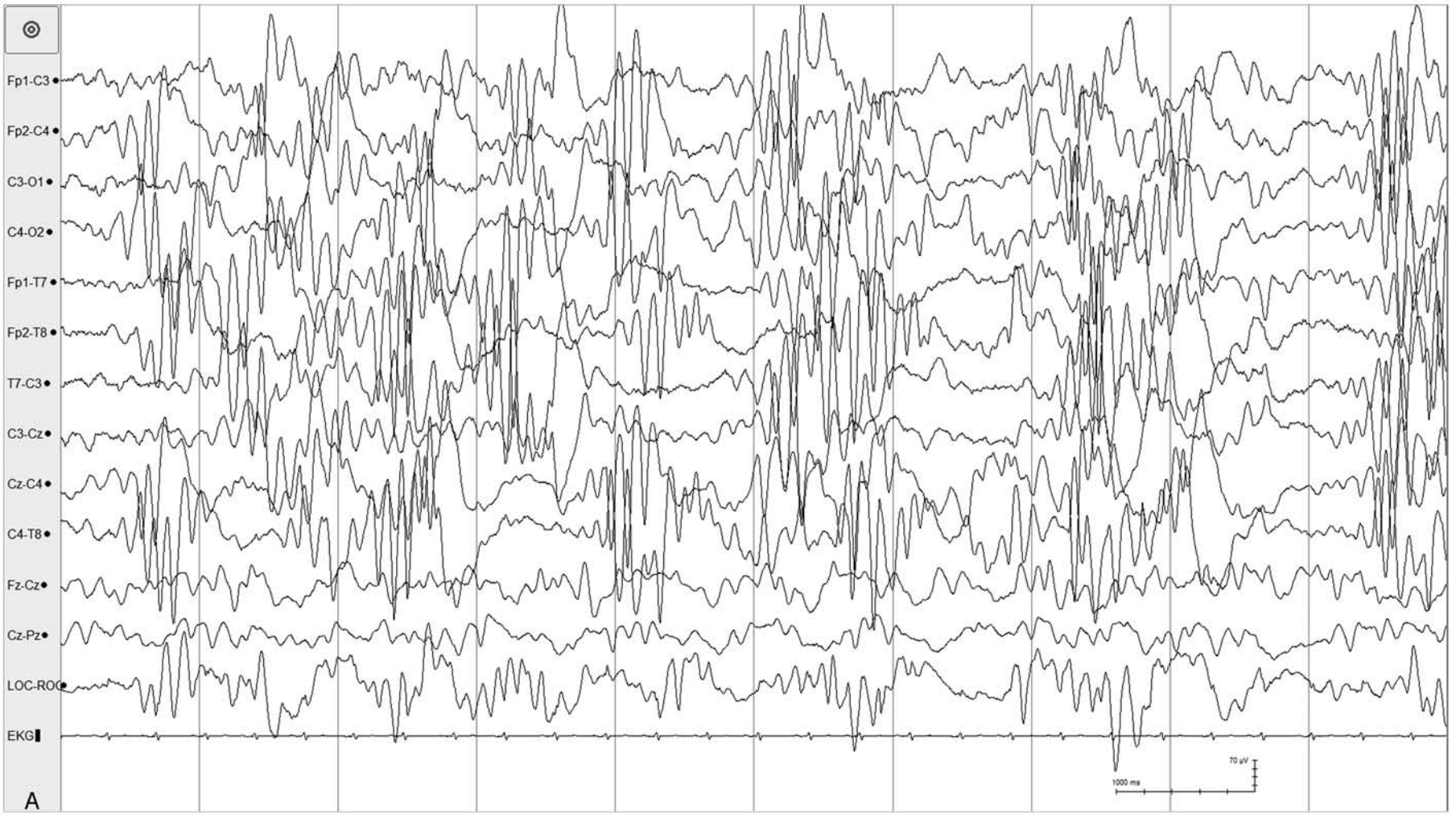


Figure 6.23 (A)–(D) Dynamic pattern of holoprosencephaly. (A) High-voltage asynchronous rhythmic alpha activity is present in all regions in this 35-week CA age infant with alobar holoprosencephaly. (*continued*)

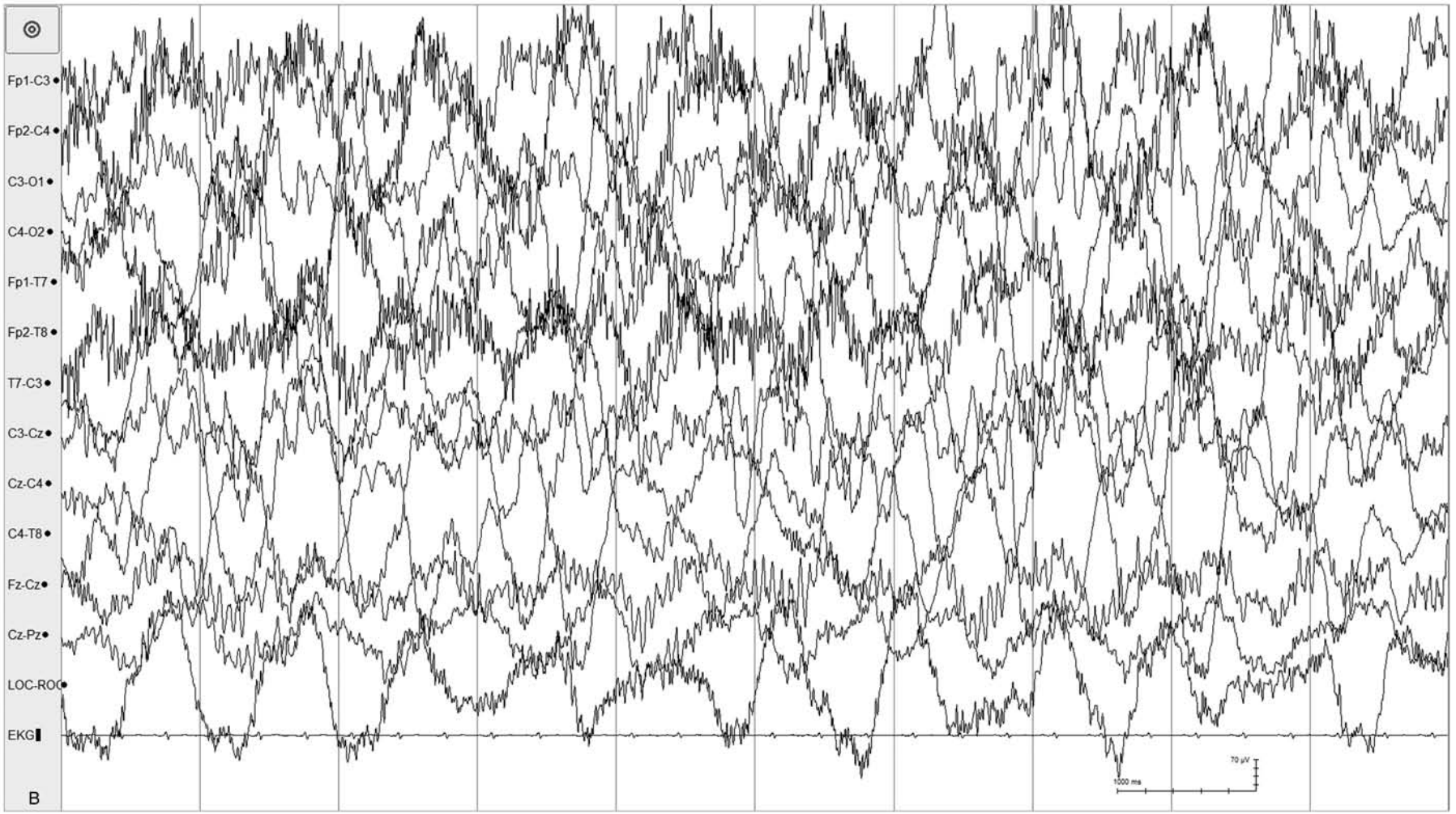


Figure 6.23 (*continued*) **(B)** High-voltage arrhythmic and asynchronous slow activity with superimposed fast activity is present in all regions in the same recording. (*continued*)

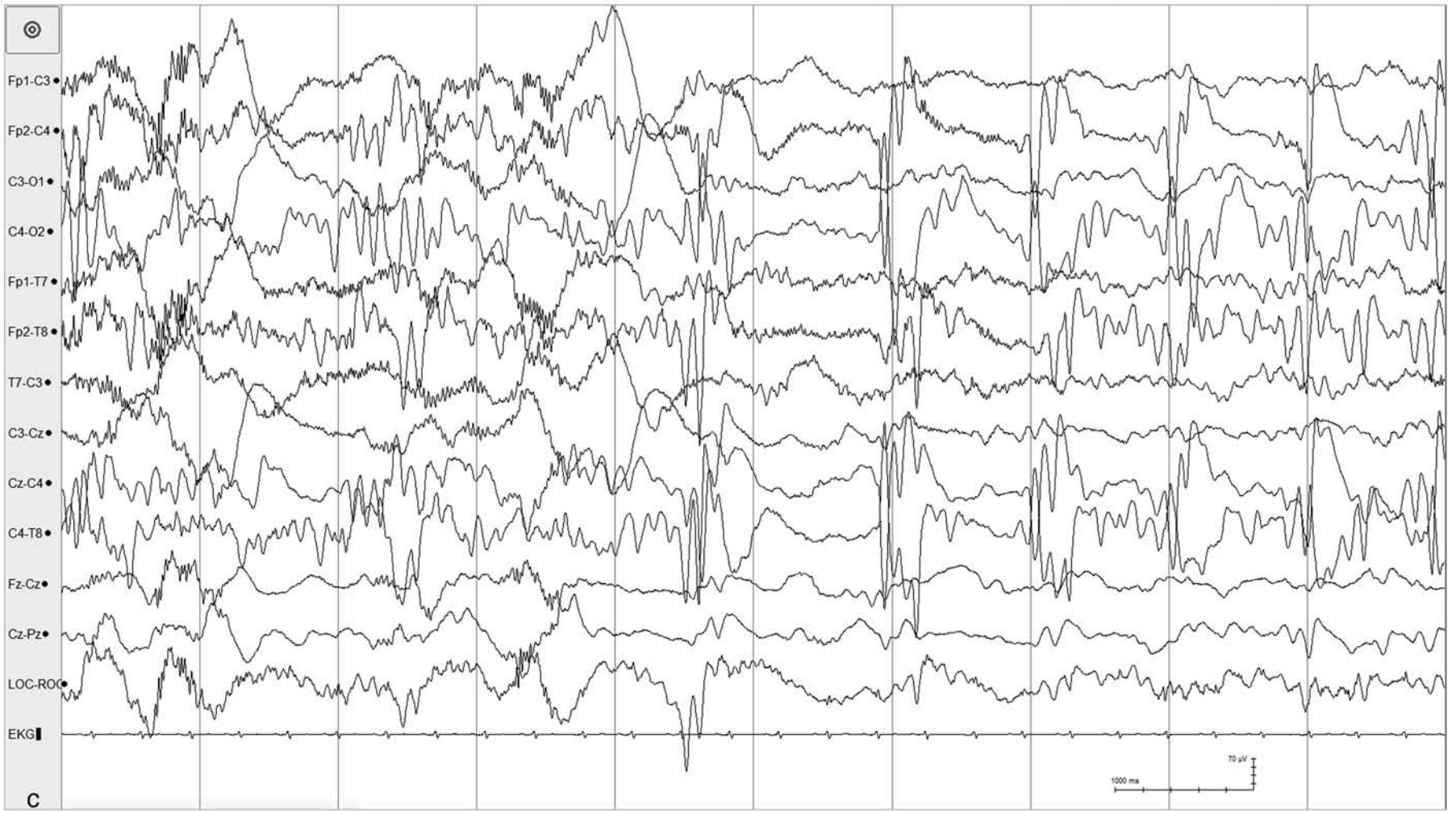


Figure 6.23 (*continued*) **(C)** Abrupt change in the character of the background from generalized asynchronous slow activity to high-voltage periodic sharp waves and rhythmic alpha activity also occurs in the same recording. (*continued*)

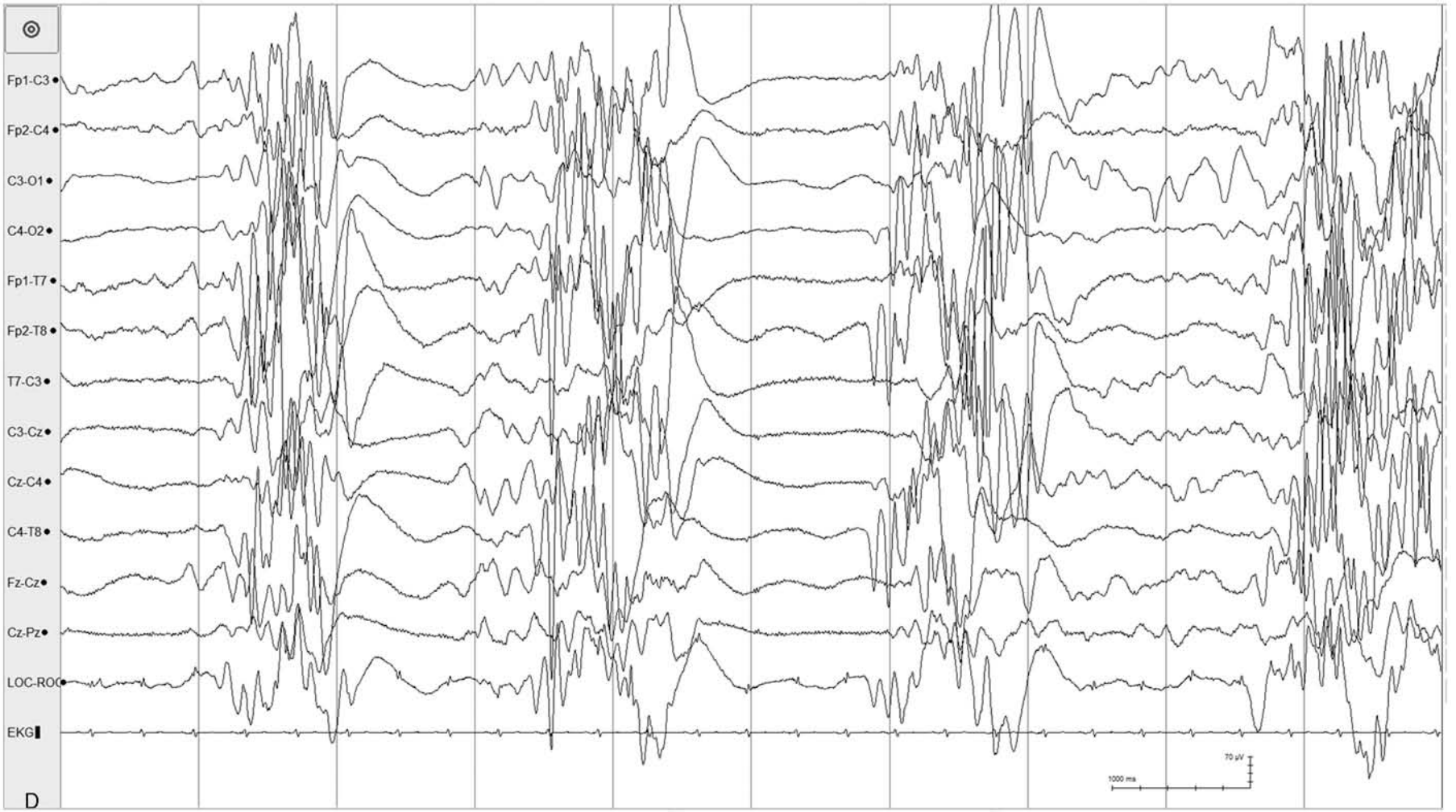


Figure 6.23 (*continued*) **(D)** Suppression-burst pattern with generalized high-voltage spike and sharp waves also occur in the same recording.

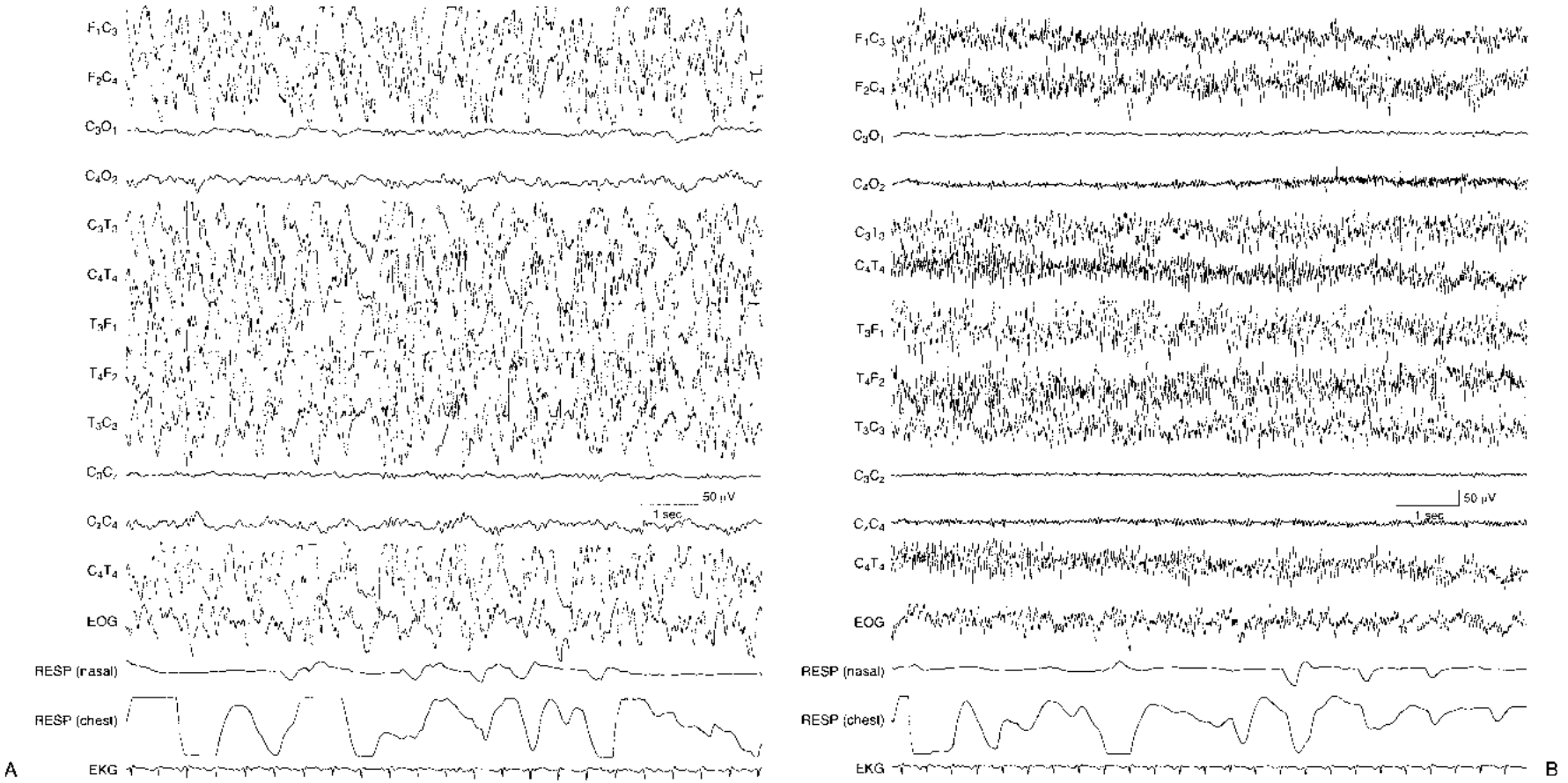


Figure 6.24 (A)–(D) Dynamic pattern of holoprosencephaly with persistent focal features. The EEG features that are typical in infants with holoprosencephaly are present in this term infant who, as part of the brain malformation, also has a dorsal cystic lesion in the occipital region that is characterized on EEG by marked depression of activity in that region. **(A)** High-voltage, rhythmic, alpha, and theta frequency activity is mixed with some slower waveforms. **(B)** High-voltage, rhythmic fast activity is present. (*continued*)

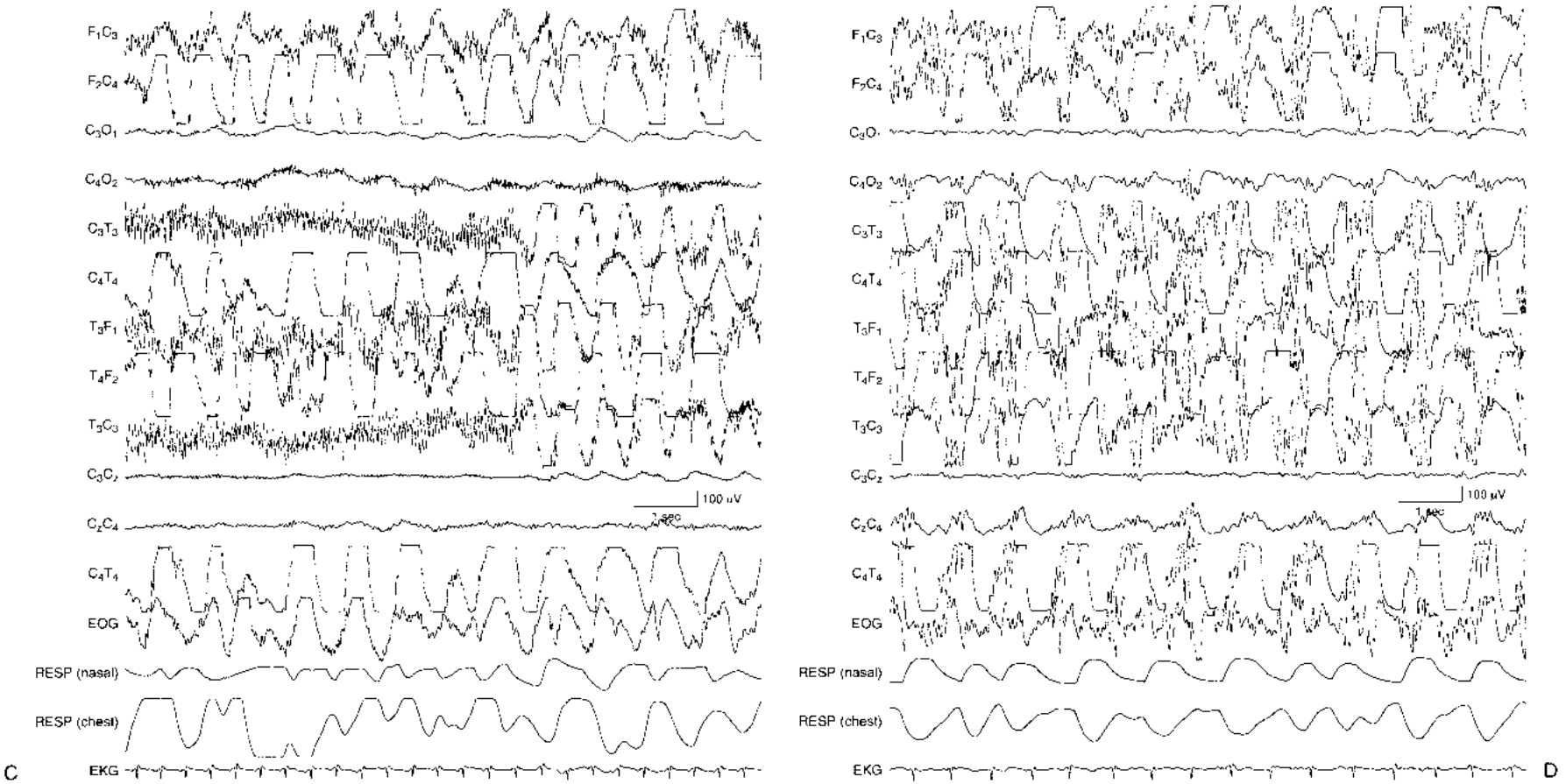


Figure 6.24 (*continued*) **(C)** High-voltage very slow activity is present on the right with the persistence of fast activity on the left until a sudden transition to slower frequencies on that side. **(D)** Asynchronous, high-voltage very slow activity with superimposed fast activity is present.

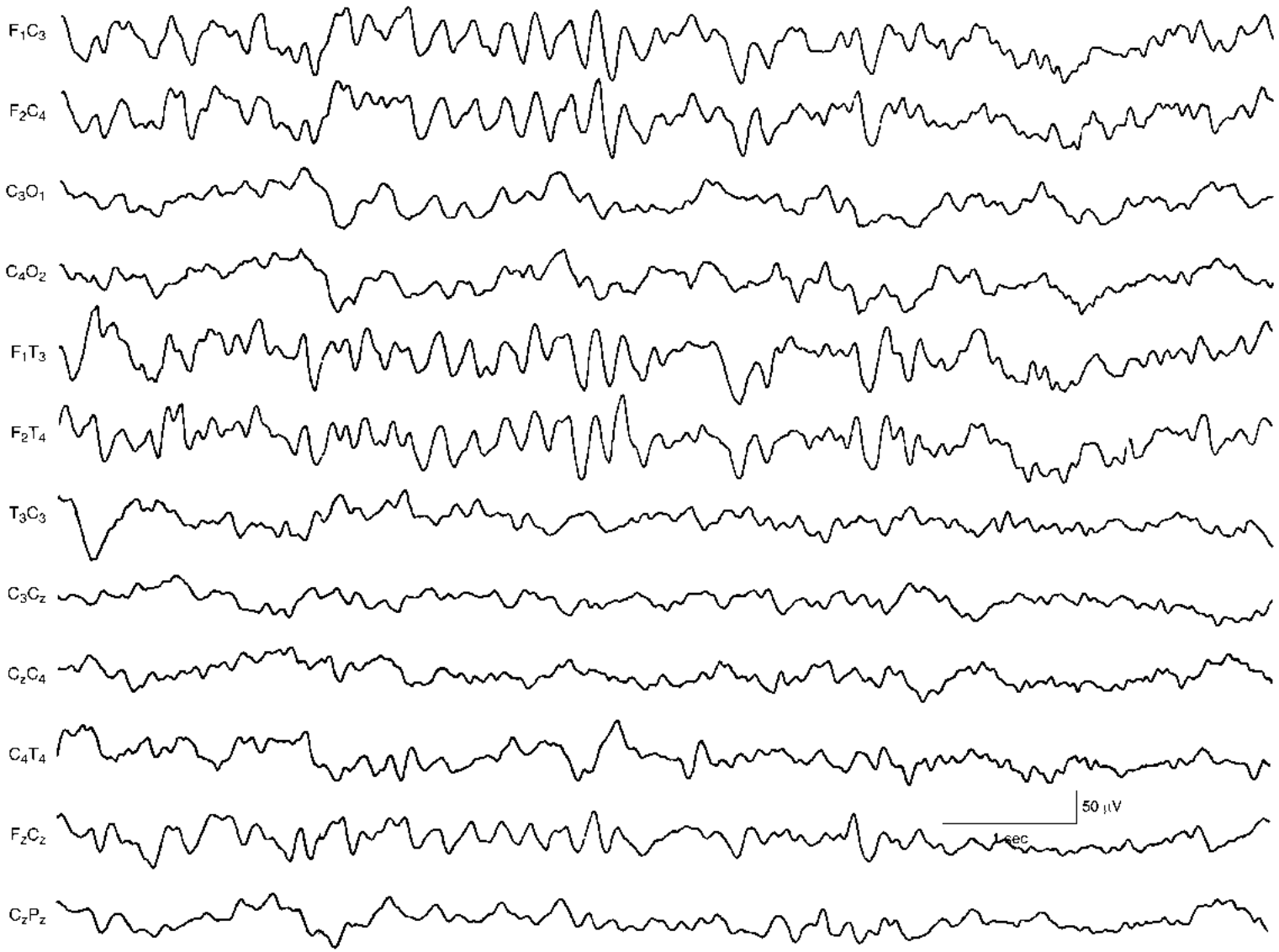


Figure 6.25 Rhythmic bifrontal theta activity. There is moderate-voltage rhythmic 5 to 6 Hz activity in the frontal regions bilaterally in this EEG that is otherwise normal in this term infant.

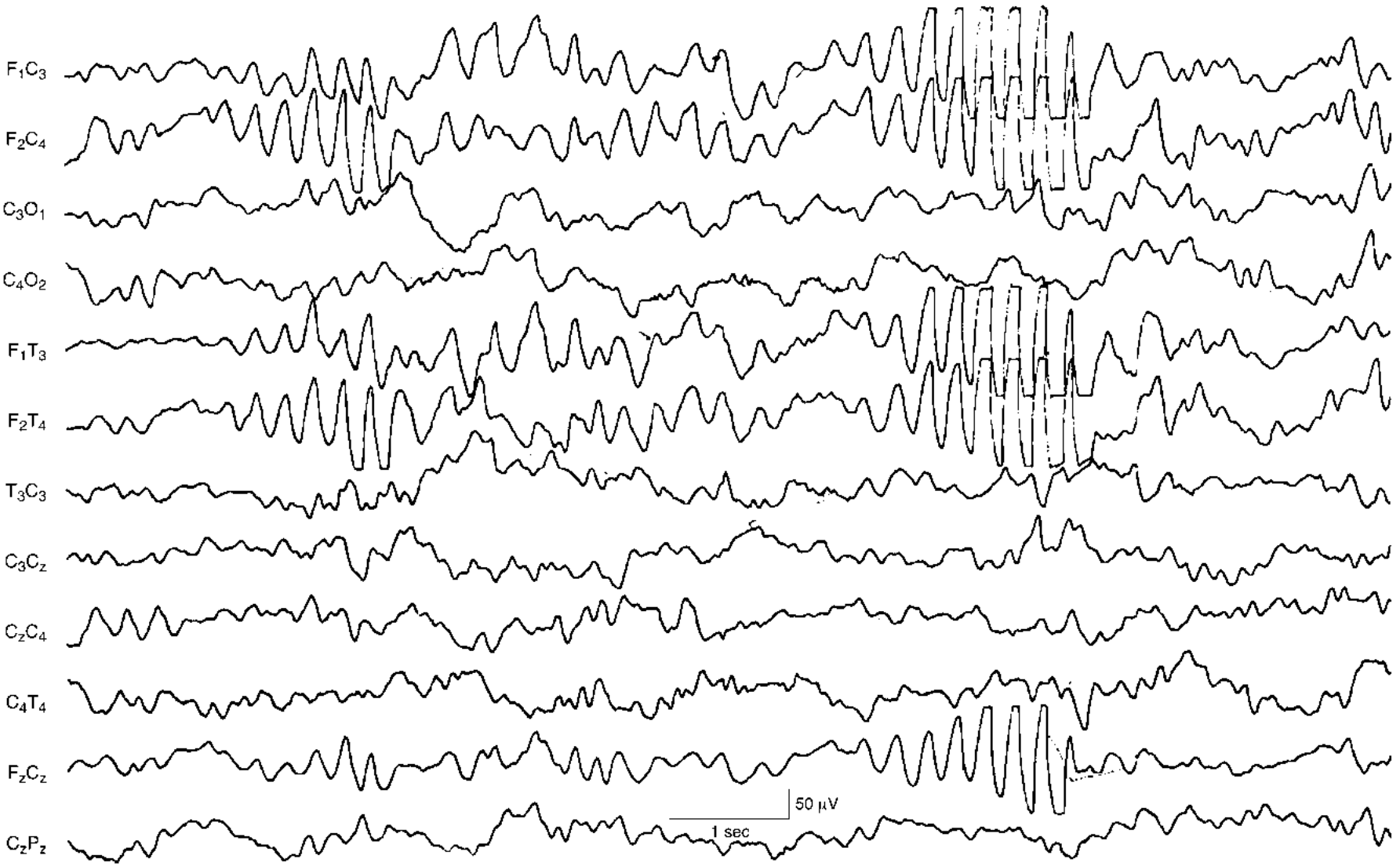


Figure 6.26 Paroxysmal bifrontal theta activity. There is paroxysmal moderately high-voltage 5 to 6 Hz activity in the frontal regions bilaterally. The EEG is otherwise normal in this term infant.

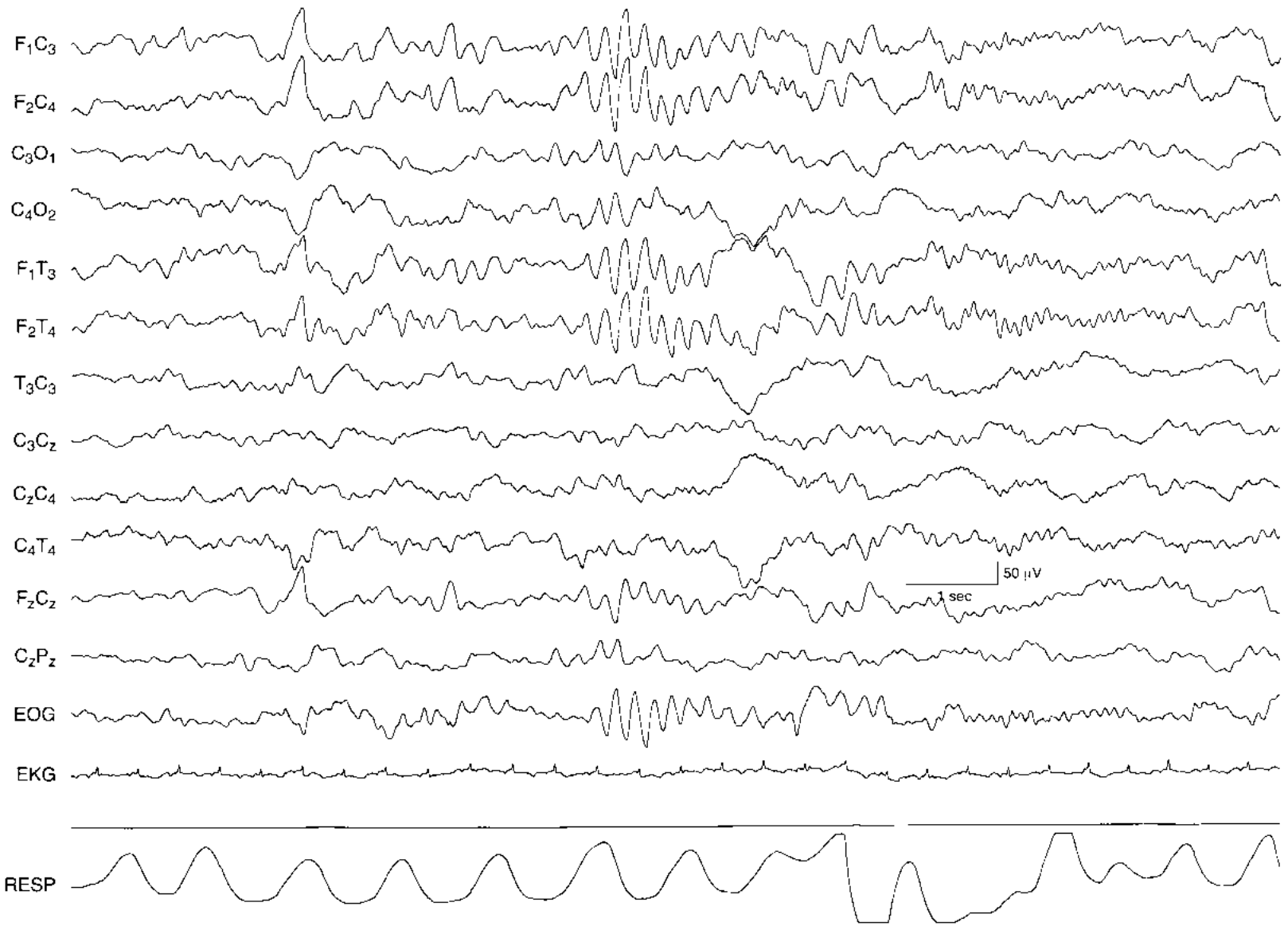


Figure 6.27 Rhythmic bifrontal theta activity followed by rhythmic bifrontal alpha activity. There is a burst of rhythmic high-voltage 5 to 6 Hz activity in the frontal regions bilaterally followed by a run of low-voltage rhythmic 8 to 9 Hz activity. The background EEG activity is otherwise normal in this term infant.

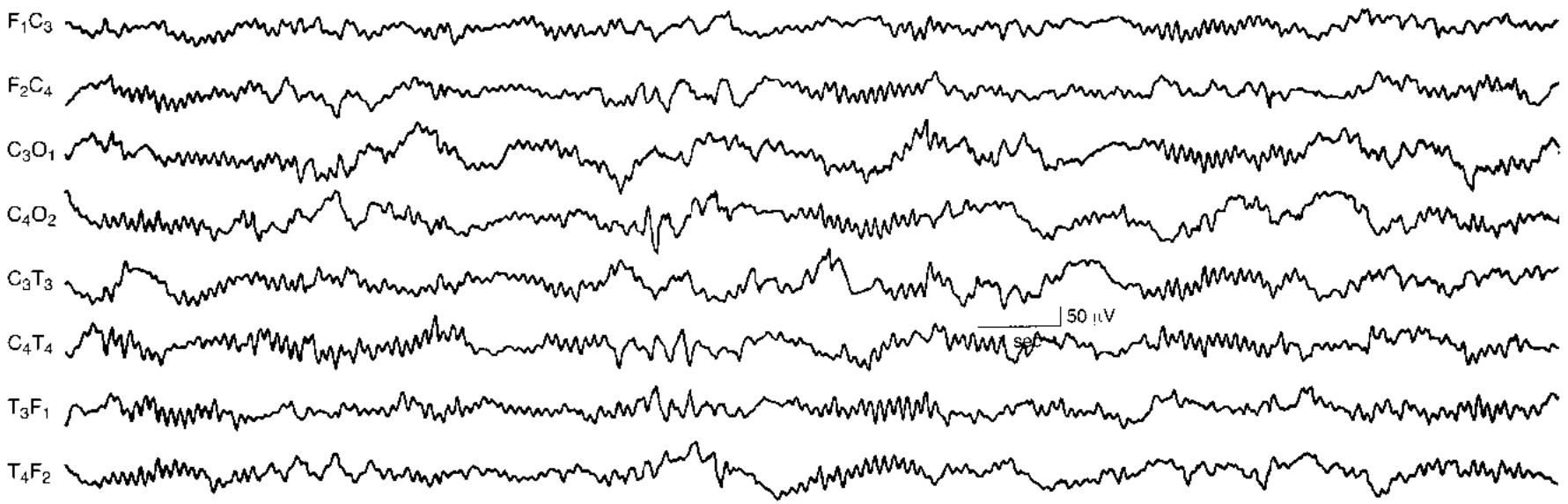


Figure 6.28 Generalized rhythmic alpha activity with variable interhemispheric asynchrony. There are runs of rhythmic 8 to 9 Hz activity occurring both synchronously and asynchronously in the left and right central regions in a term infant with a chromosomal abnormality and multiple congenital anomalies. (Hrachovy et al., 1990, with permission.)

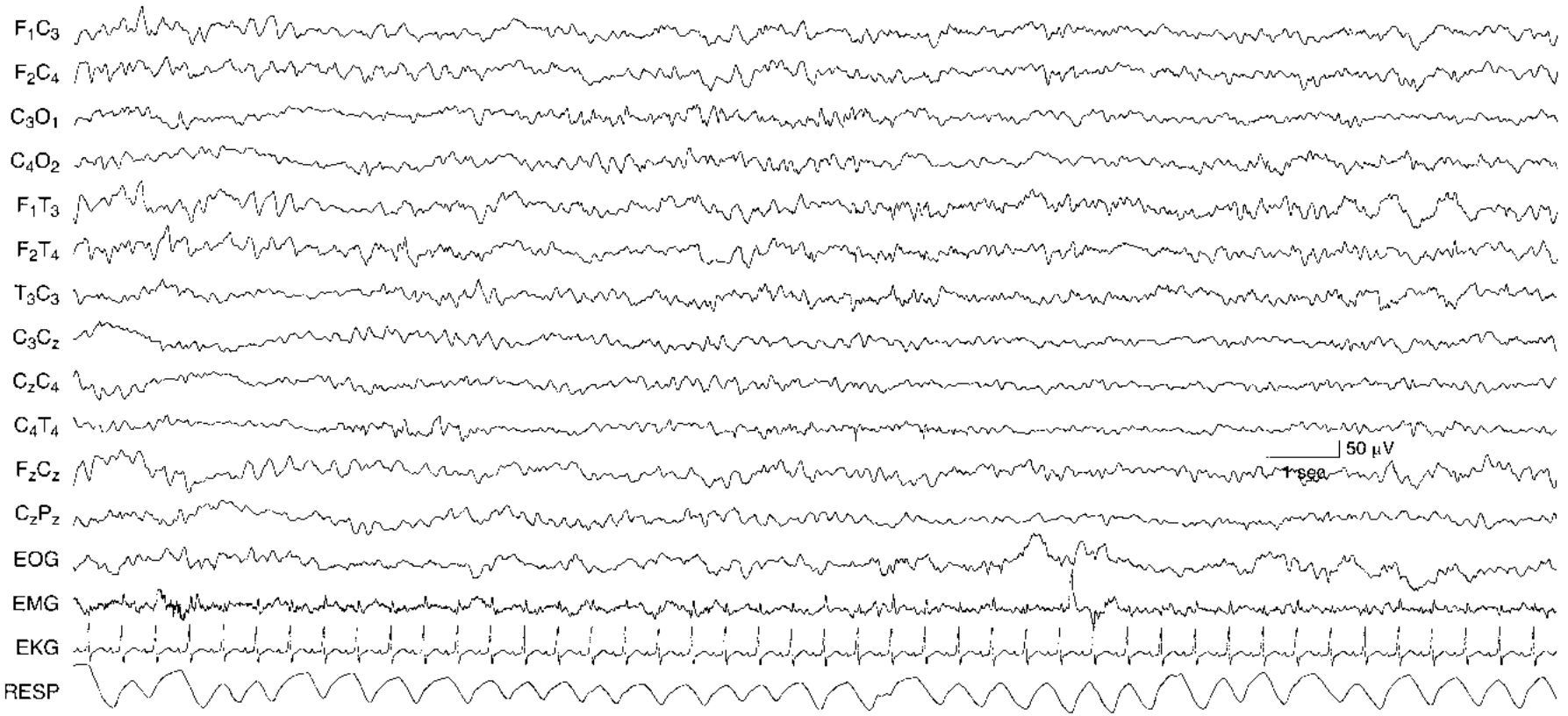


Figure 6.29 Generalized rhythmic alpha and theta activity. There are runs of 8 to 9 Hz activity mixed with 5 to 6 Hz activity in all regions in the EEG of this term infant with congenital heart disease.

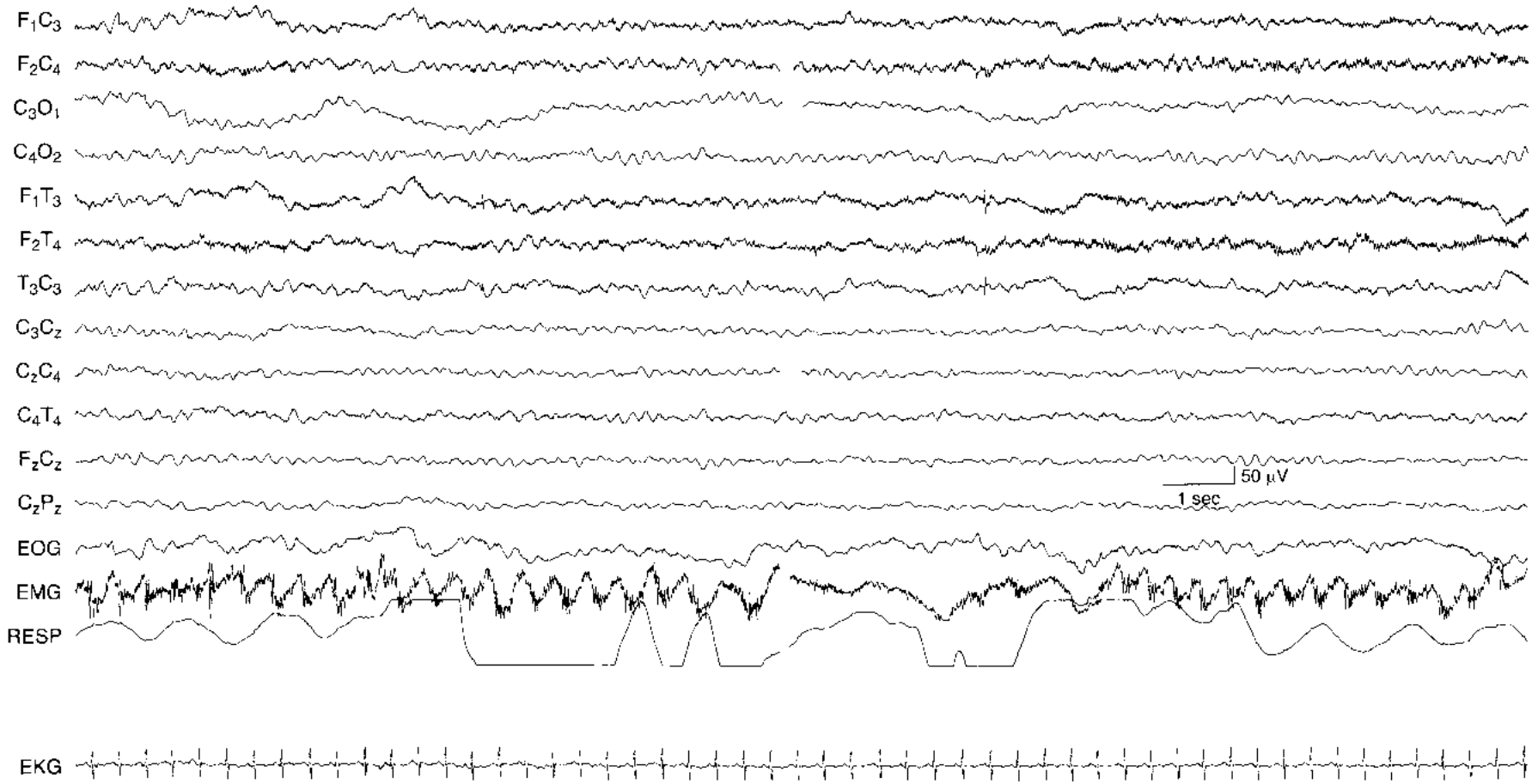


Figure 6.30 Generalized rhythmic theta activity. There is sustained, monomorphic, rhythmic 5 to 6 Hz activity chiefly in the anterior regions in this term infant with the inborn error of metabolism, citrullinemia.

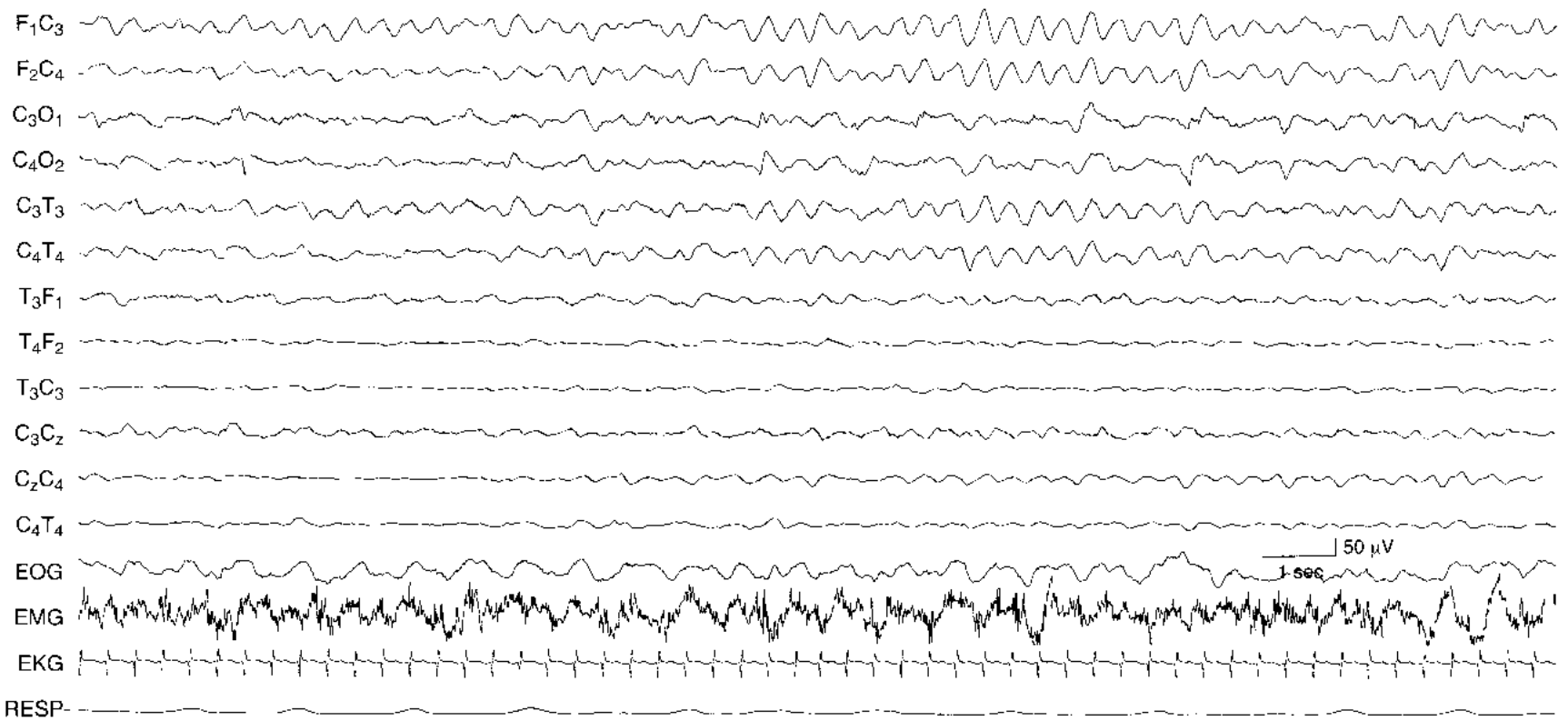


Figure 6.31 Rhythmic, monomorphic, bifrontal delta activity. There are monorhythmic, monomorphic, 2.5 to 3 Hz activity in the frontal regions bilaterally and the background activity is depressed in this term infant with nonaccidental head injury.

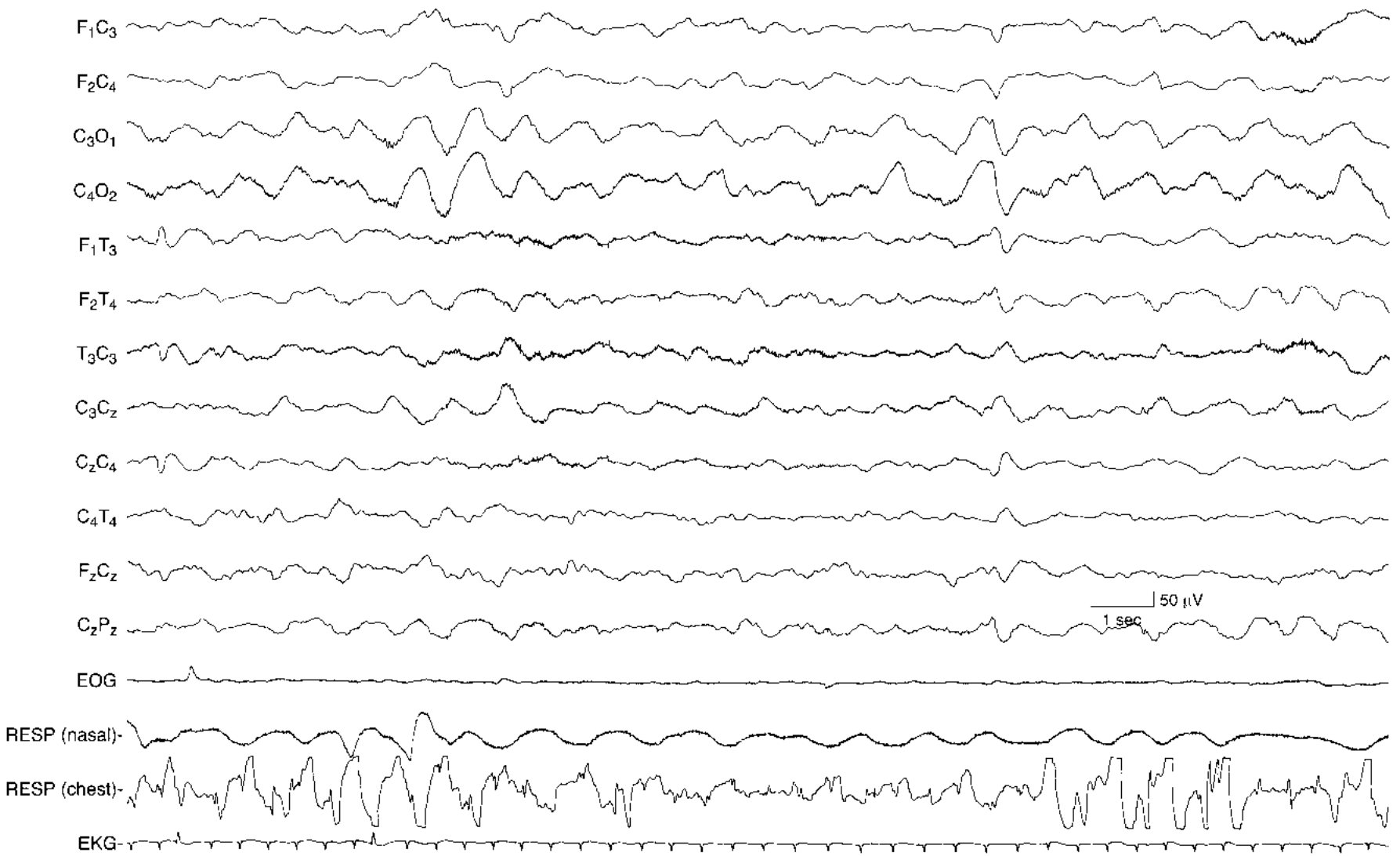


Figure 6.32 Rhythmic bioccipital slow activity. There is high-voltage, 1 to 1.5 Hz activity in the occipital regions of the EEG of this term infant. The background activity is undifferentiated.

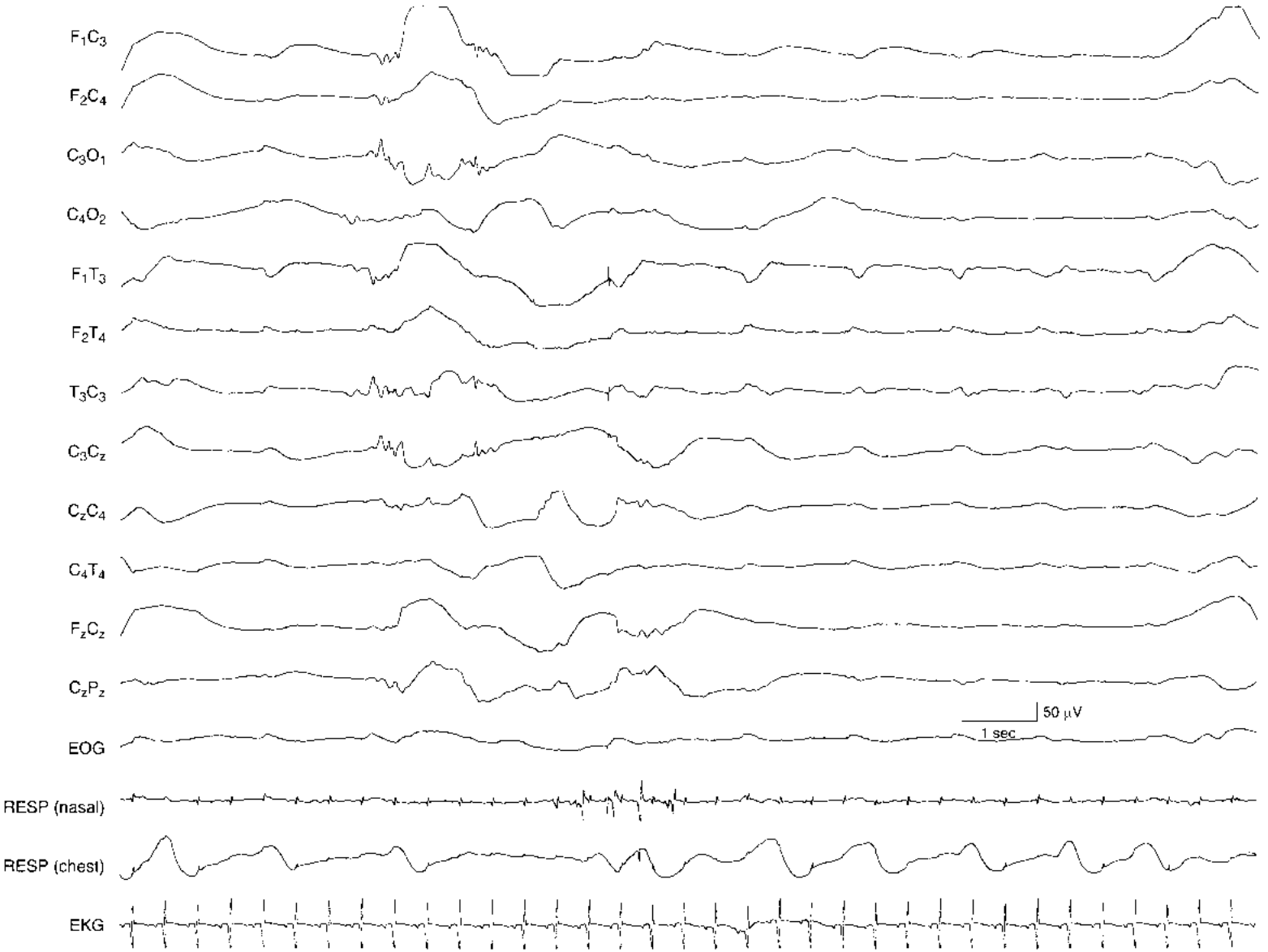


Figure 6.33 Periodic lateralized discharges associated with herpes simplex virus encephalitis (HSVE). Low voltage, slow transients recur periodically in the left temporal region in this term infant with HSVE. The background activity is depressed and undifferentiated and there are randomly occurring low voltage sharp waves in the left central region.

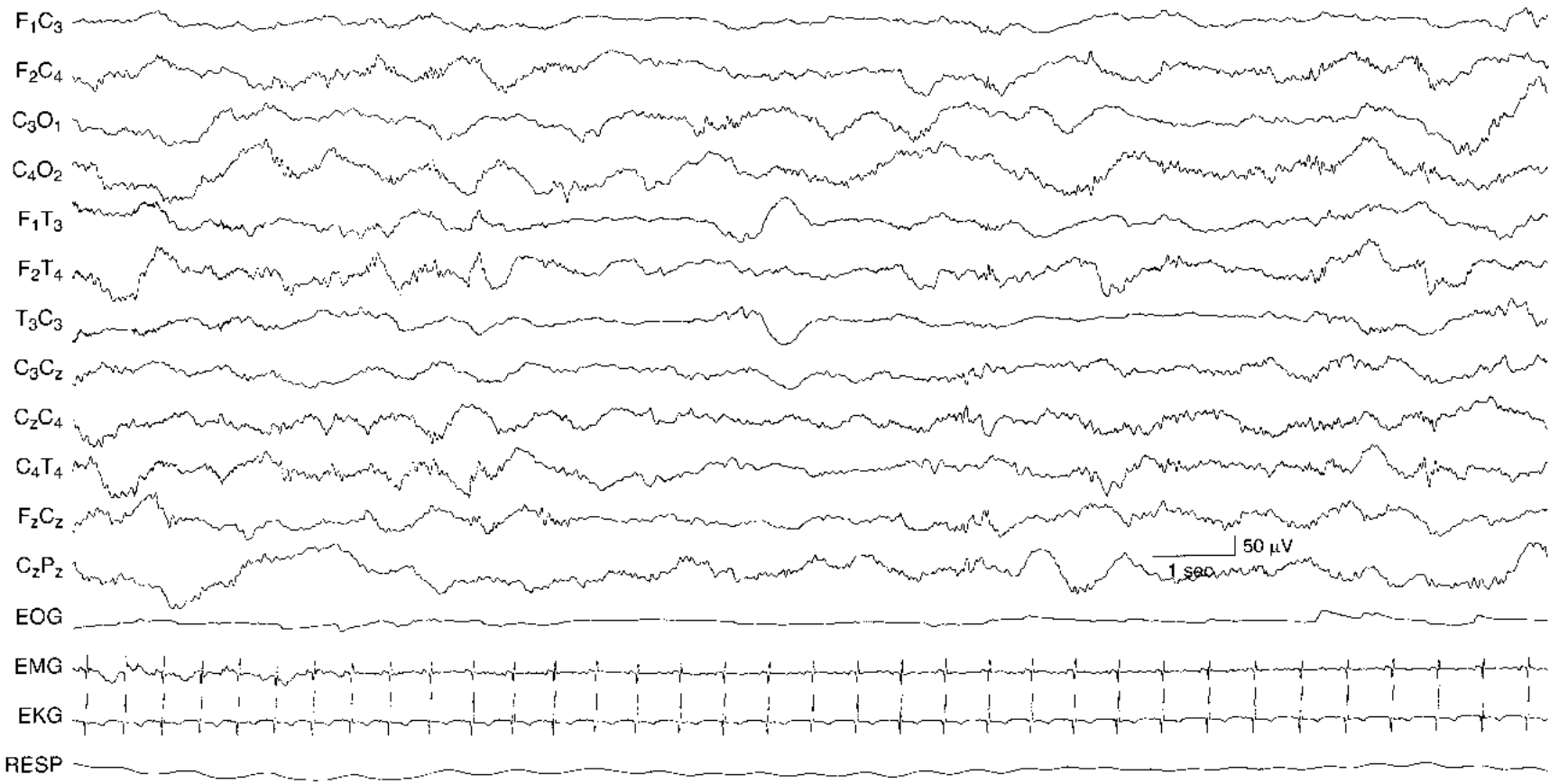


Figure 6.34 Voltage asymmetry. There is a voltage asymmetry with the amplitude of waves lower in the leads from the left hemisphere compared to the right. The background activity on the right shows beta–delta complexes. This 35 to 36 weeks CA infant had a left fronto-parietal intracerebral hemorrhage and an IVH with involvement of the germinal matrix on the left.

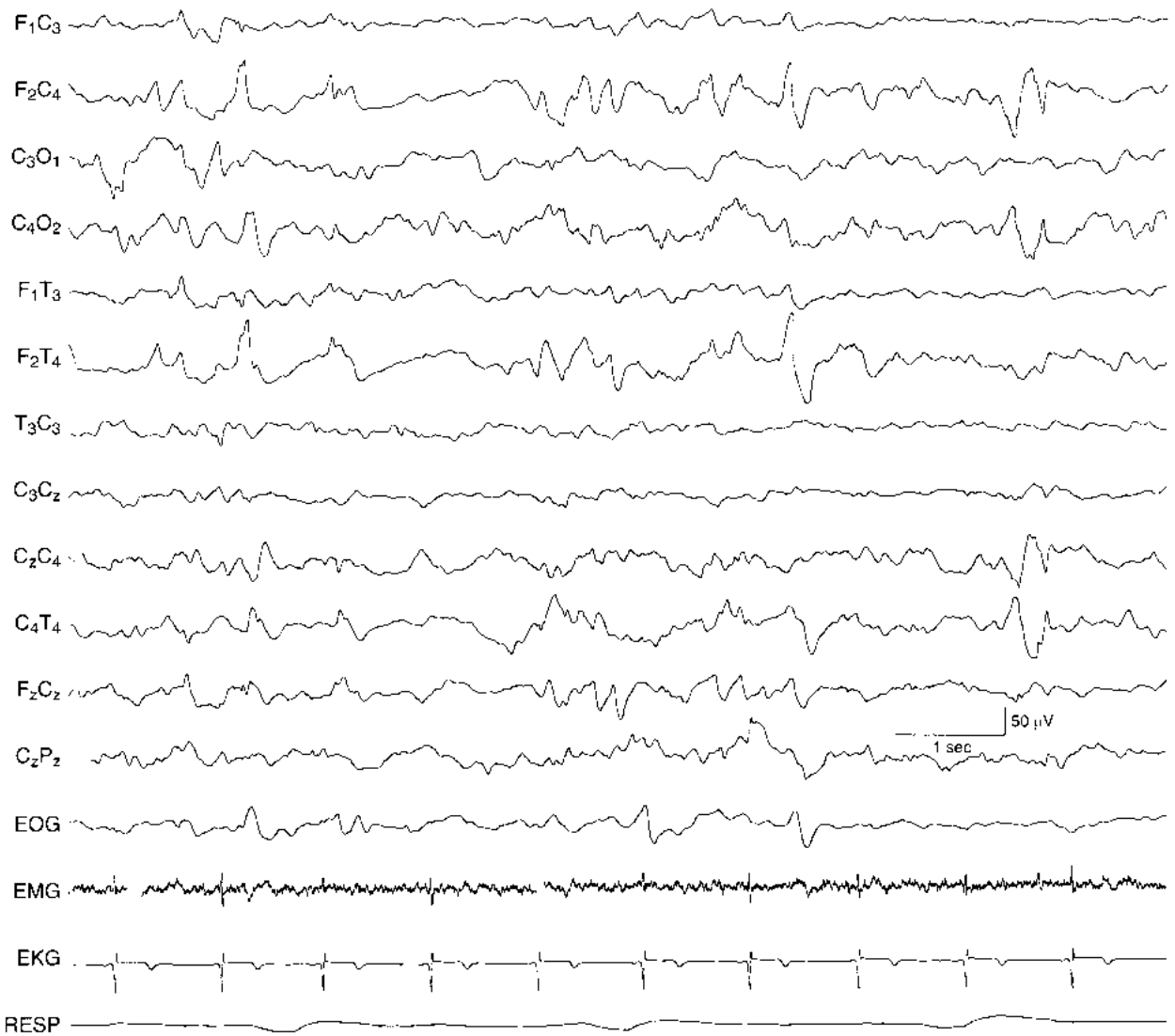


Figure 6.35 Voltage asymmetry with mildly abnormal background activity. There is a voltage asymmetry with the amplitude of waves lower on the left compared to homologous regions on the right. Although frontal sharp transients—normal developmental milestones—persist on the right, the background activity is abnormal with little activity of fast frequency and a greater than expected amount of slower waves. This term infant suffered a left frontoparietal intracerebral hemorrhage.

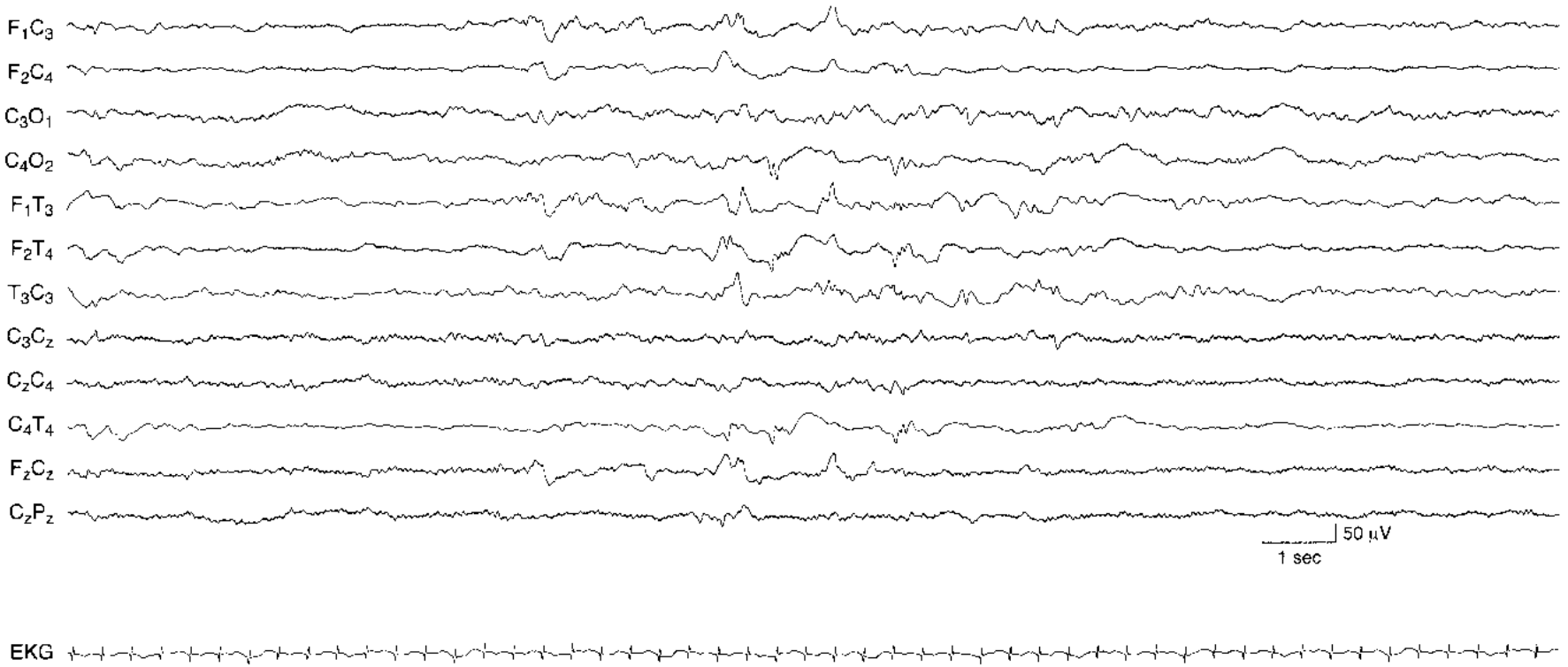


Figure 6.36 Voltage asymmetry associated with abnormal background activity. There is a voltage asymmetry with the amplitude of waves lower in leads from the right central-temporal hemisphere compared to homologous regions on the left. Random moderate-voltage sharp waves are present bilaterally. The background activity is low in voltage. The infant is term with a right parietal infarction and diagnosis of hypoxic-ischemic encephalopathy.

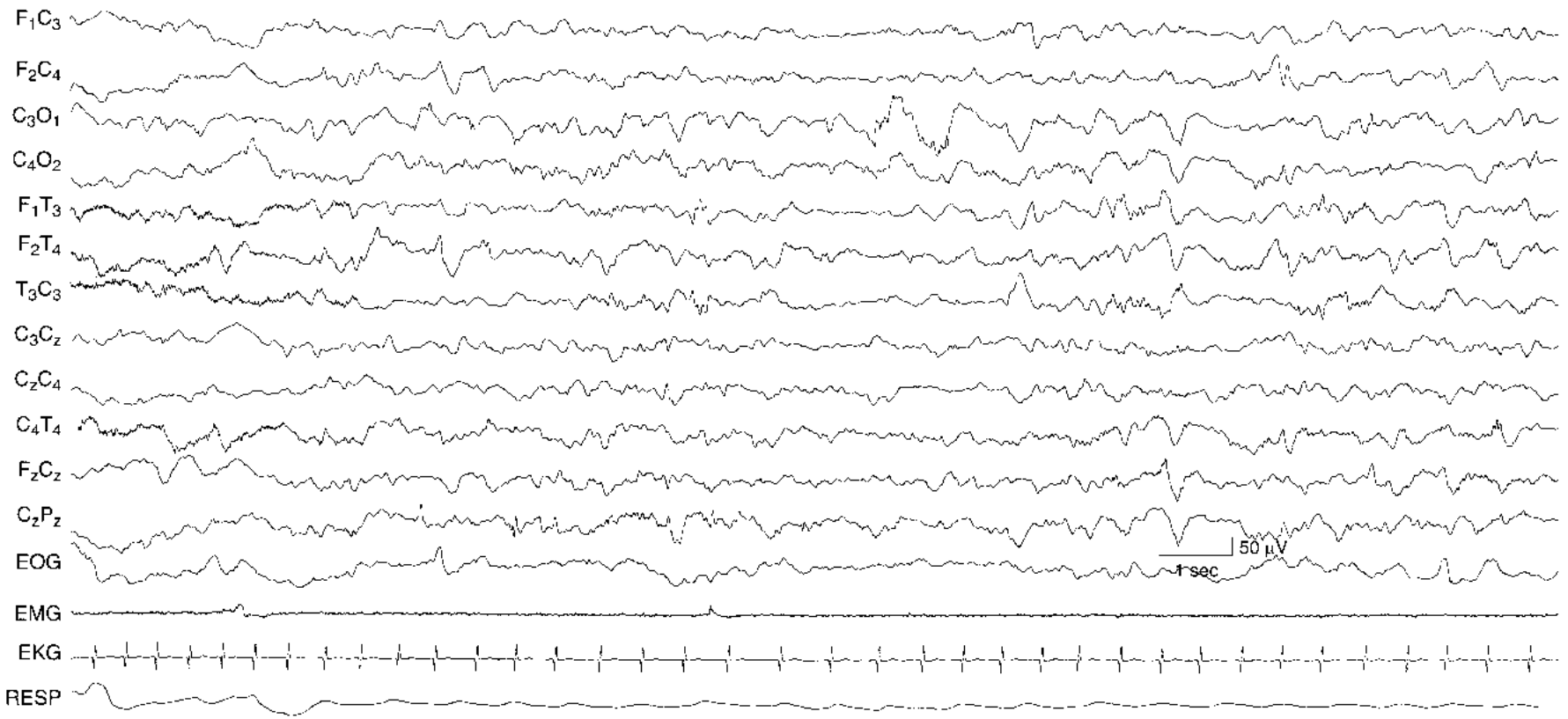


Figure 6.37 Focal slow activity in the left occipital region. There is moderate to moderately high-voltage 1 to 3 Hz activity in the left occipital region in this term infant with a congenital cystic lesion in that region.

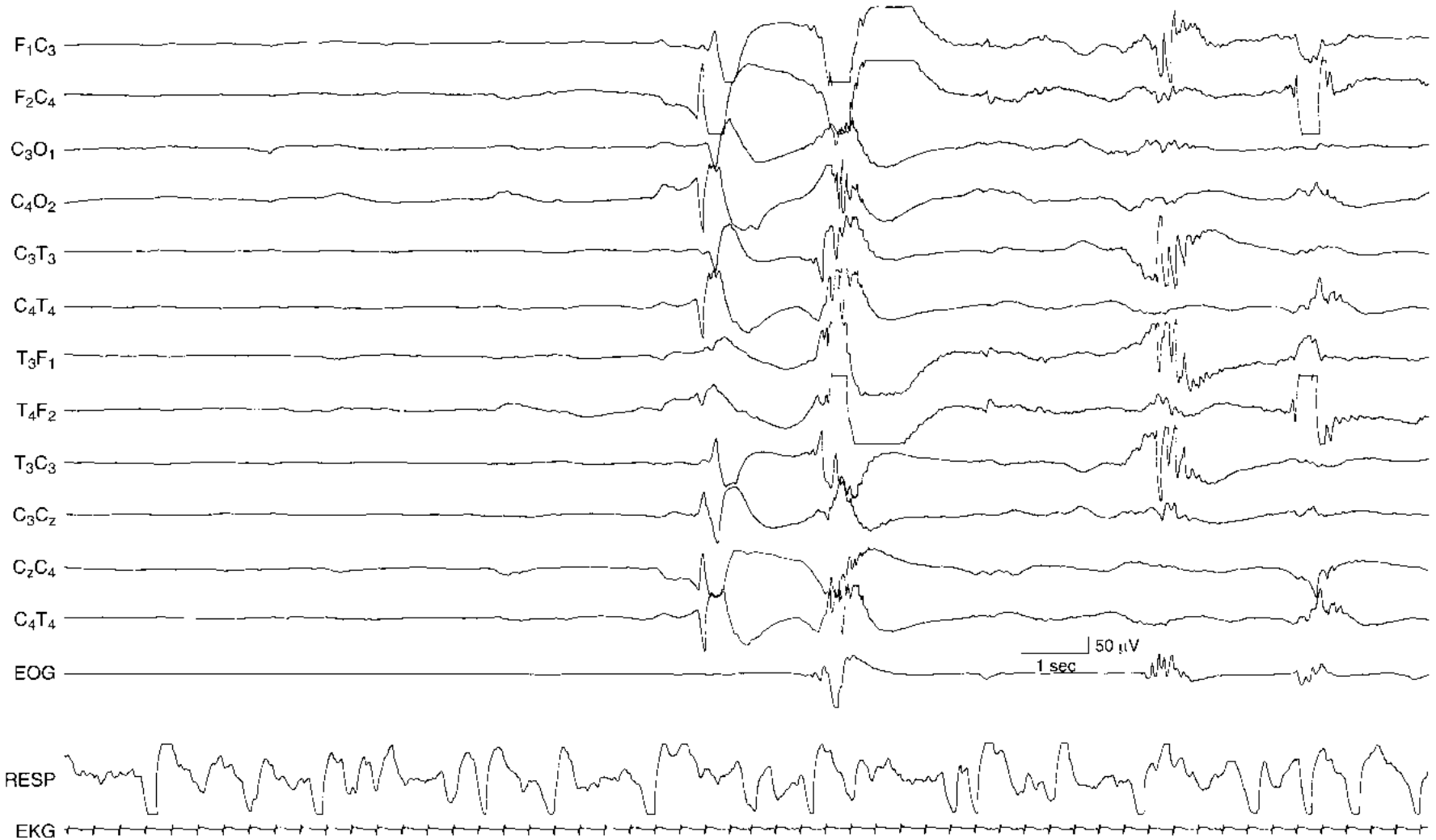


Figure 6.38 Surface positive sharp waves in the premature. After a period of quiescence a high-voltage surface positive sharp wave is present in the right central region. This is followed by abnormal spike and sharp wave activity a few seconds later. Eventually, a temporal theta burst—a normal feature—is present. This EEG is from a 29- to 30-week CA infant with an IVH.

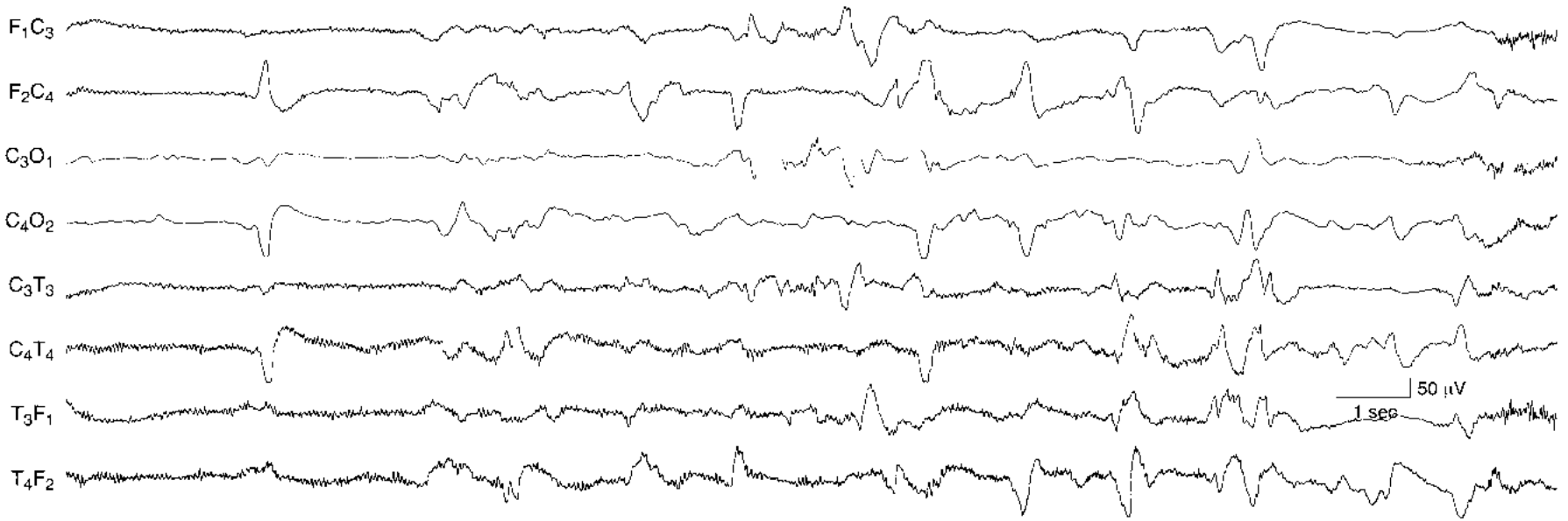


Figure 6.39 Occurrence and location of surface positive sharp waves. Surface positive sharp waves may appear as a unilateral, single transient wave as in the early portion of this sample. They may also recur at a relatively frequent rate and appear asynchronously on the two sides as in the later portion of this sample. This sample is taken from the EEG of a 36-week CA infant with IVH. The background activity is depressed and undifferentiated; there is filtered EMG artifact present in the frontal and temporal leads.

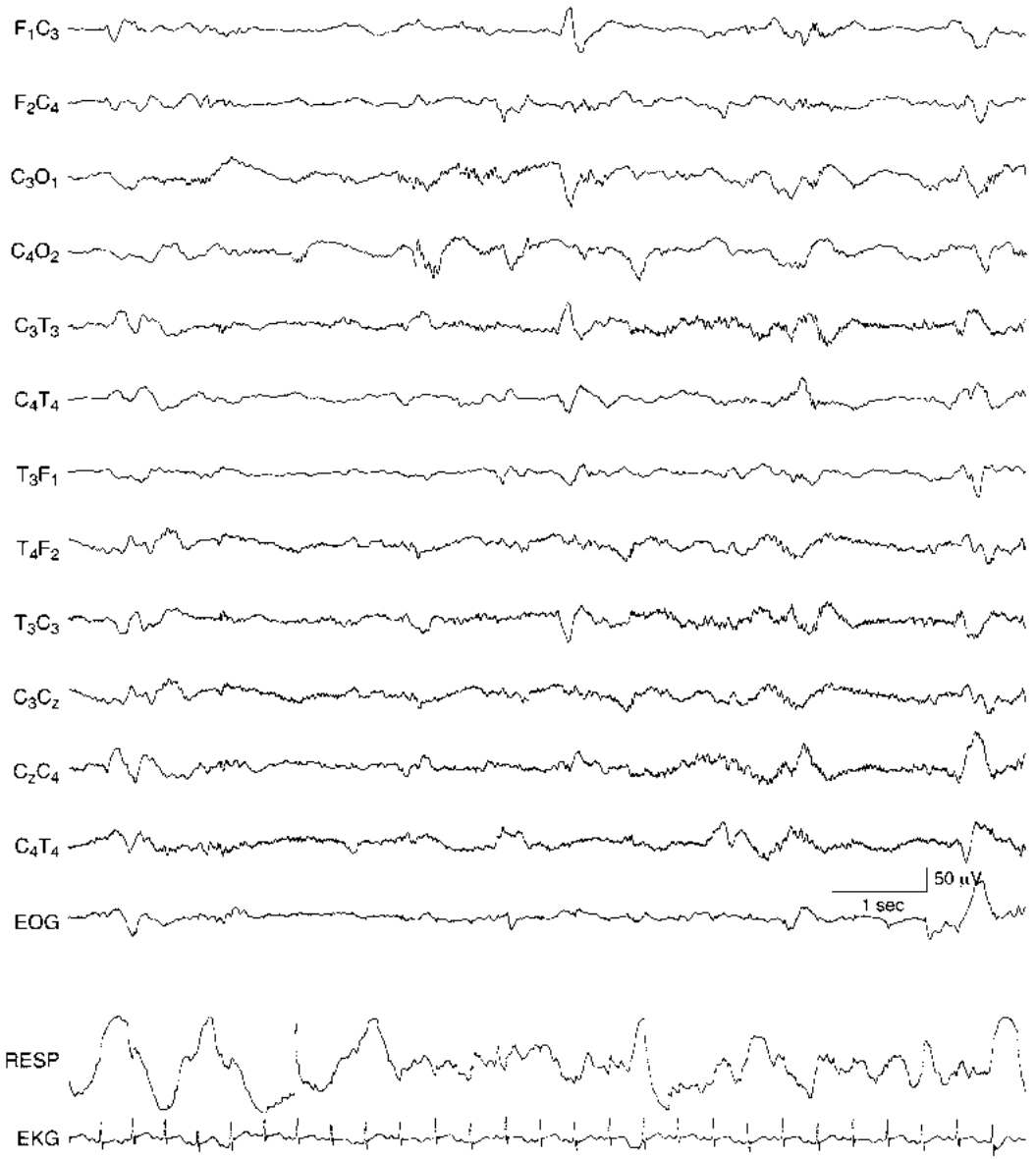


Figure 6.40 Surface positive sharp waves with moderate voltage. A surface positive sharp wave of moderate voltage is present in the left central region. The background EEG activity is within the range of normal variation and consistent with 34 to 35 weeks CA in this infant with periventricular leukomalacia.

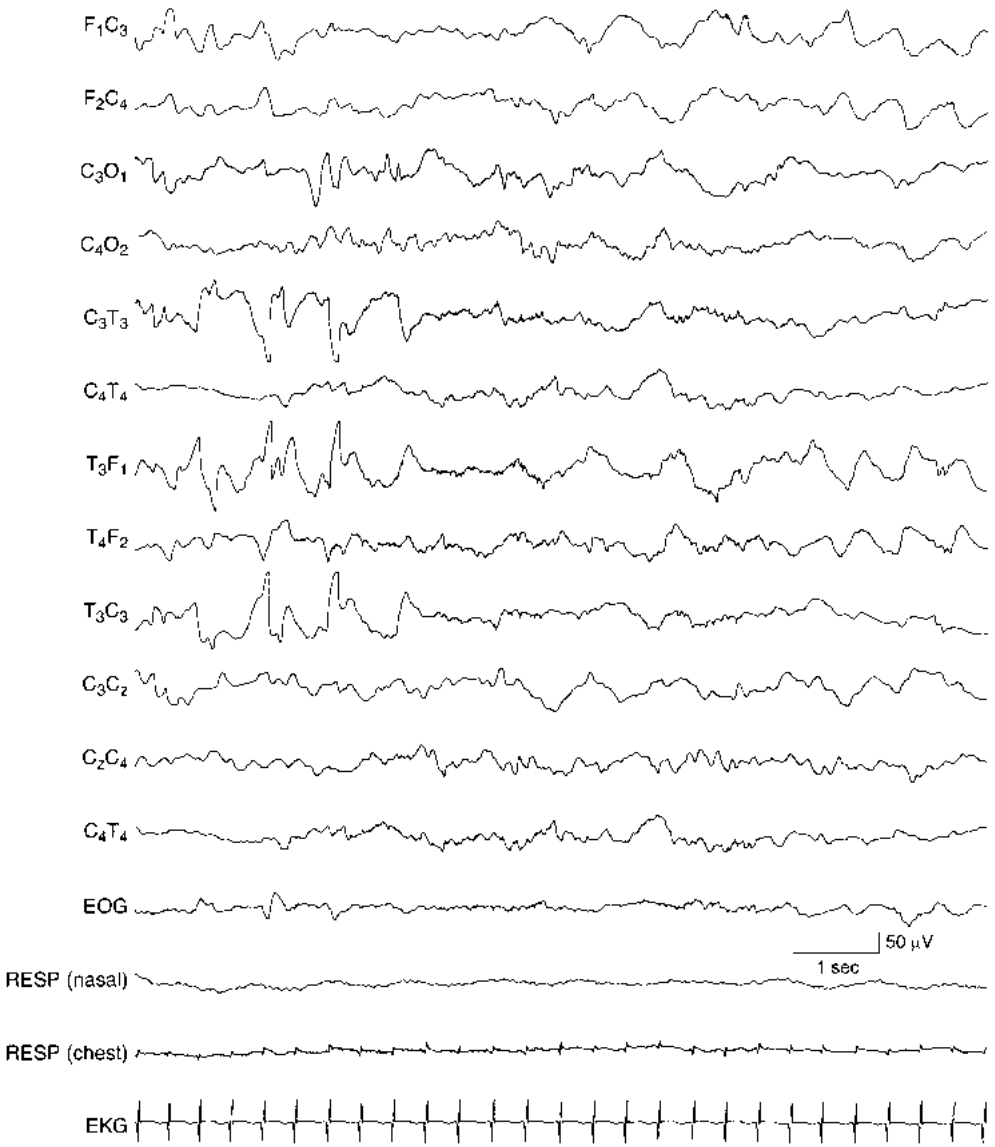


Figure 6.41 Temporal sharp waves with complex morphology. Abnormal temporal sharp waves with complex morphology are present in the left temporal region in the early portion of this sample of a term infant. The background EEG activity is normal and includes some intermittent, rhythmic delta activity in the frontal regions bilaterally. (See Chapter 5 for additional samples of abnormal temporal sharp waves.)

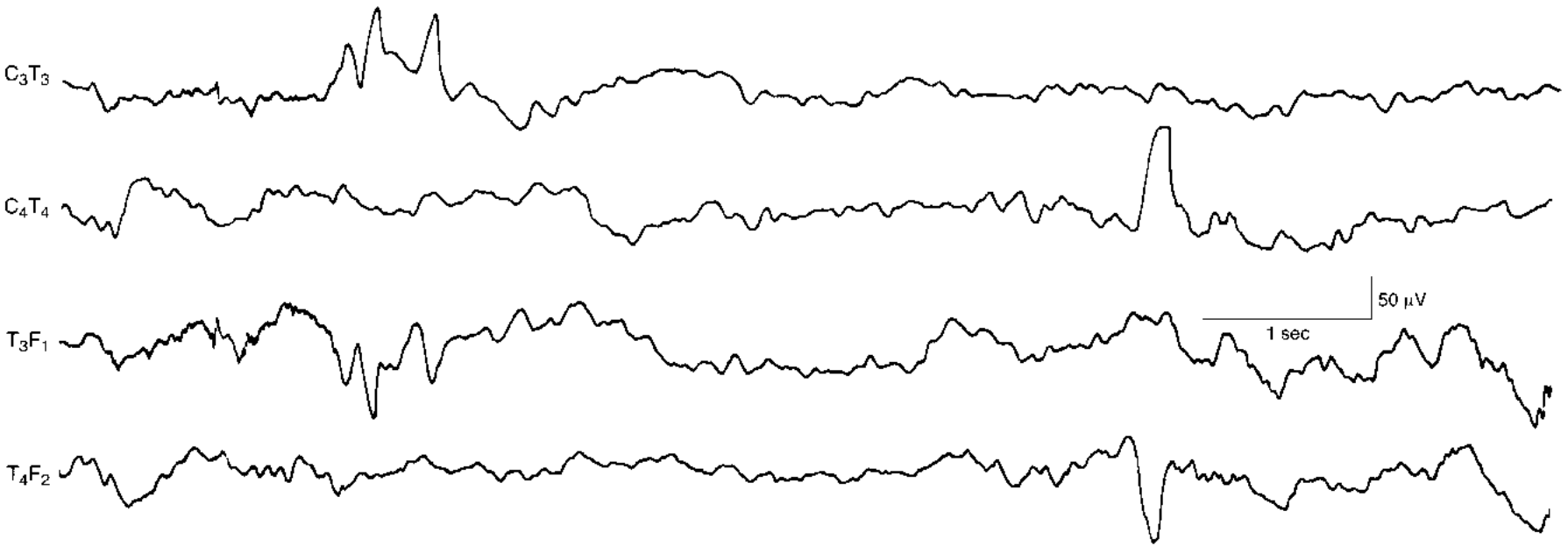


Figure 6.42 Surface positive temporal sharp waves. During the second half of this EEG sample, there is an abnormal surface positive high-voltage sharp wave in the right temporal region. Earlier, there are moderate-voltage temporal sharp waves that are repetitive with both surface positive and surface negative components. This sample is selected from a standard 12-channel EEG recording. (Hrachovy et al., 1990, with permission.)

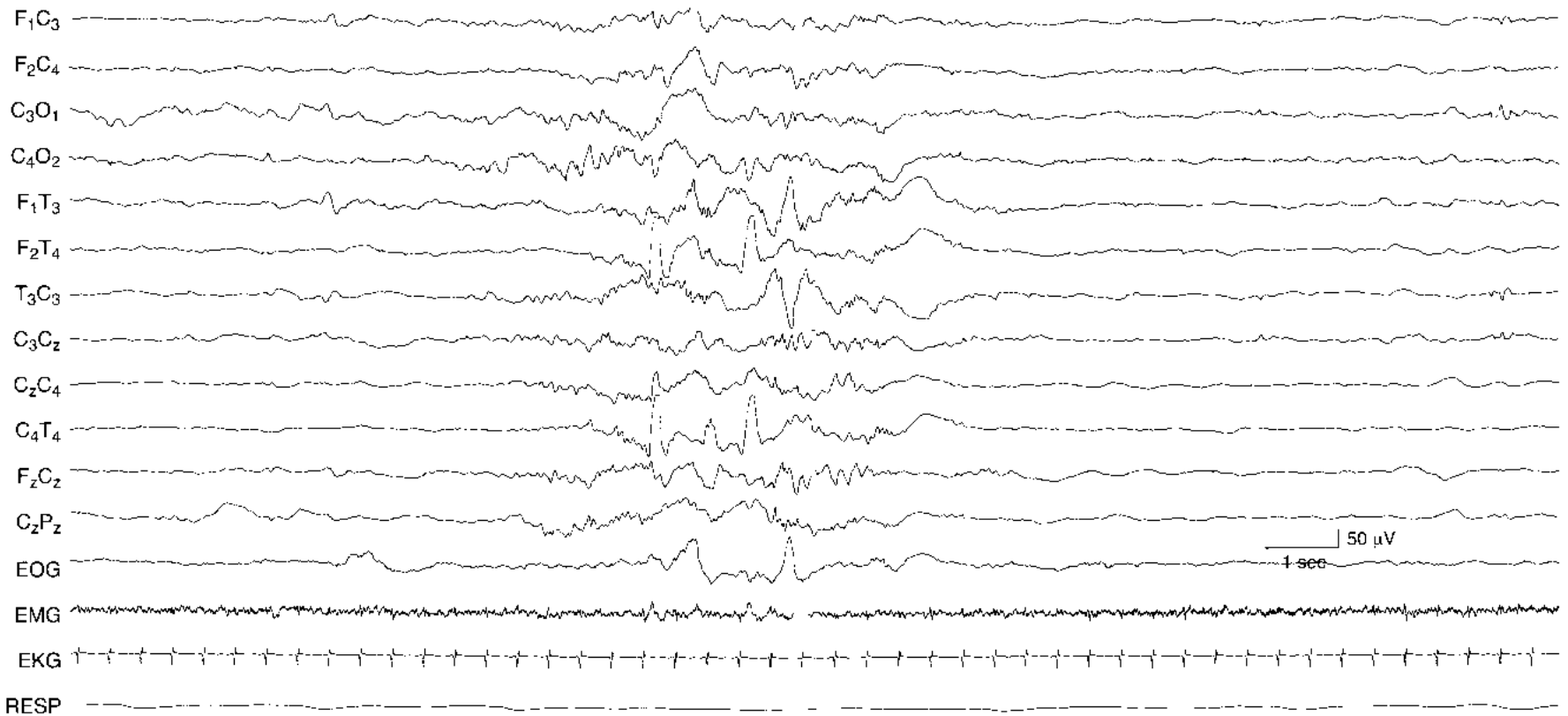


Figure 6.43 Asynchronous, independent surface positive temporal sharp waves. Surface positive sharp waves are present independently in the left and right temporal regions in this 35-week CA infant with a chromosomal abnormality, dysmorphic features, and germinal matrix hemorrhage.

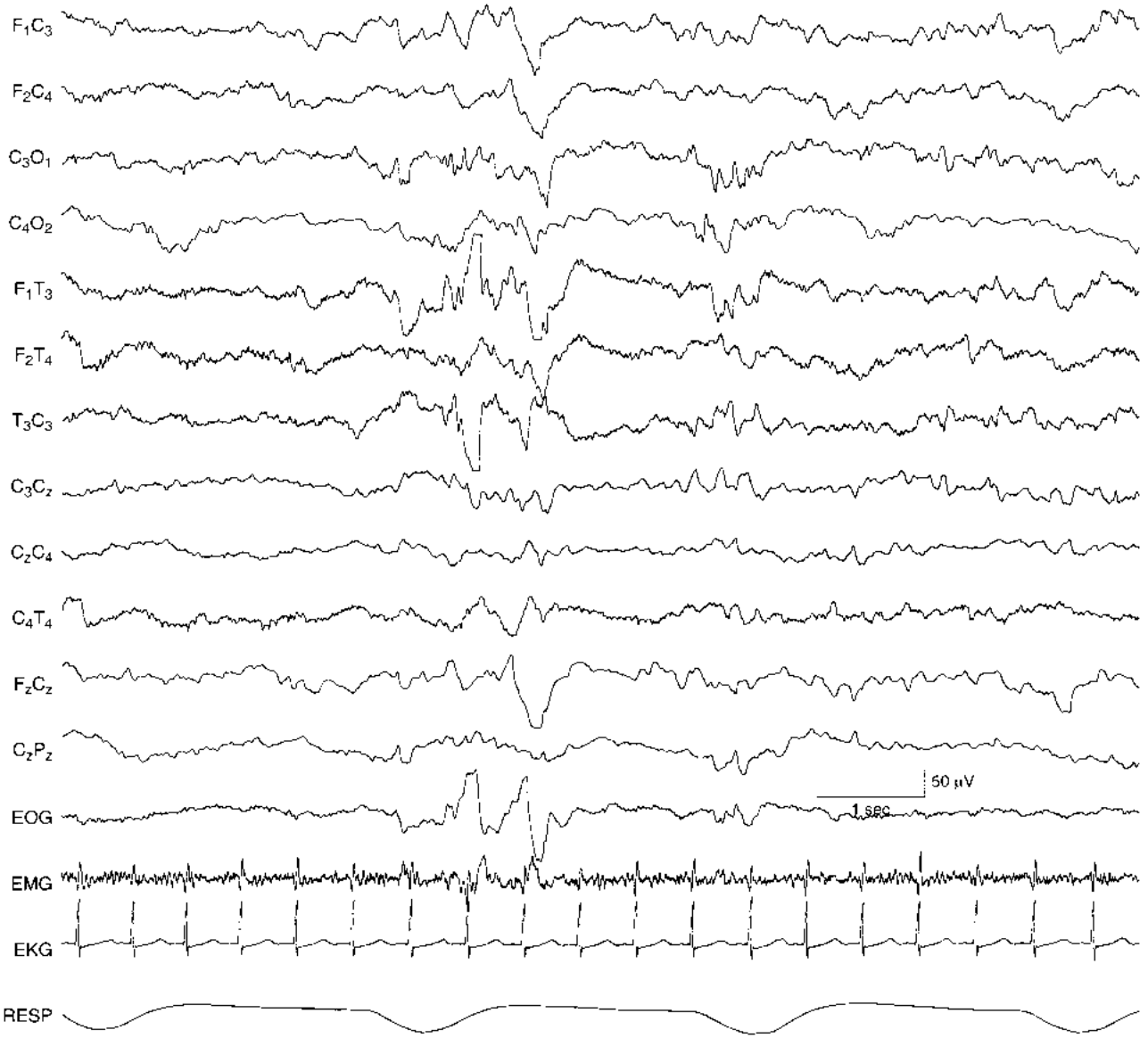


Figure 6.44 Surface positive sharp waves in the temporal region with complex morphology. A sharp wave with both surface positive and surface negative components is present in the left temporal region in this 40-week CA infant with an intracerebral hemorrhage in the left temporal lobe.

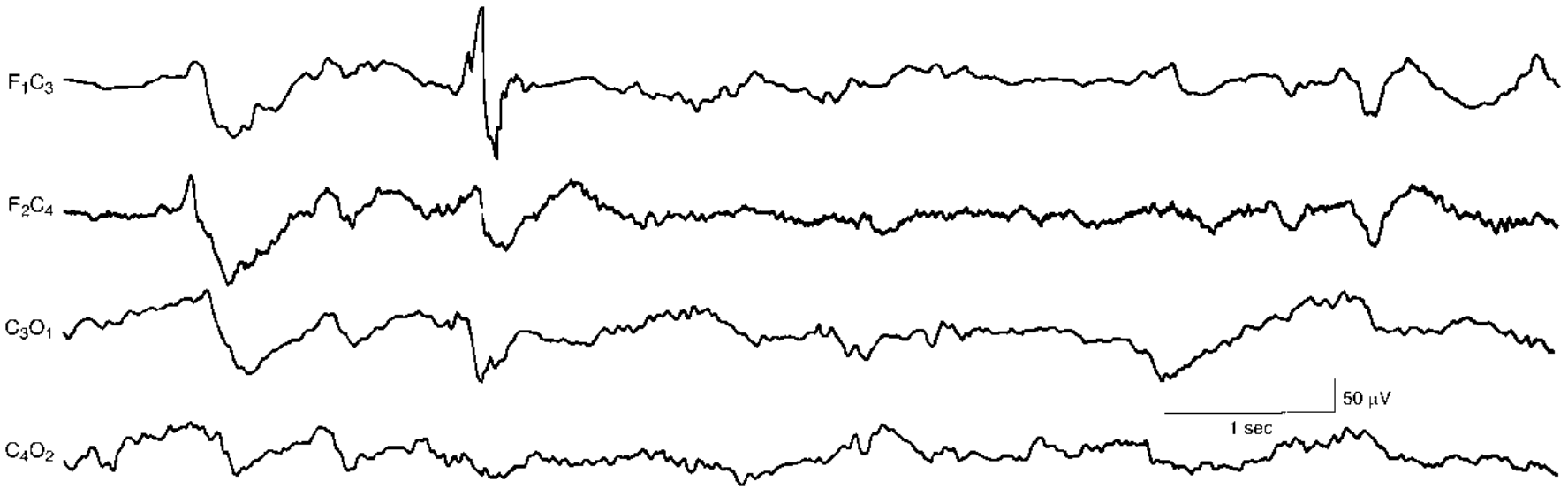


Figure 6.45 Abnormal frontal sharp waves. There is an abnormal sharp wave, with polyphasic morphology, in the left frontal region in this term infant. This is a selected sample from a 12-channel EEG. (Hrachovy et al., 1990, with permission.)

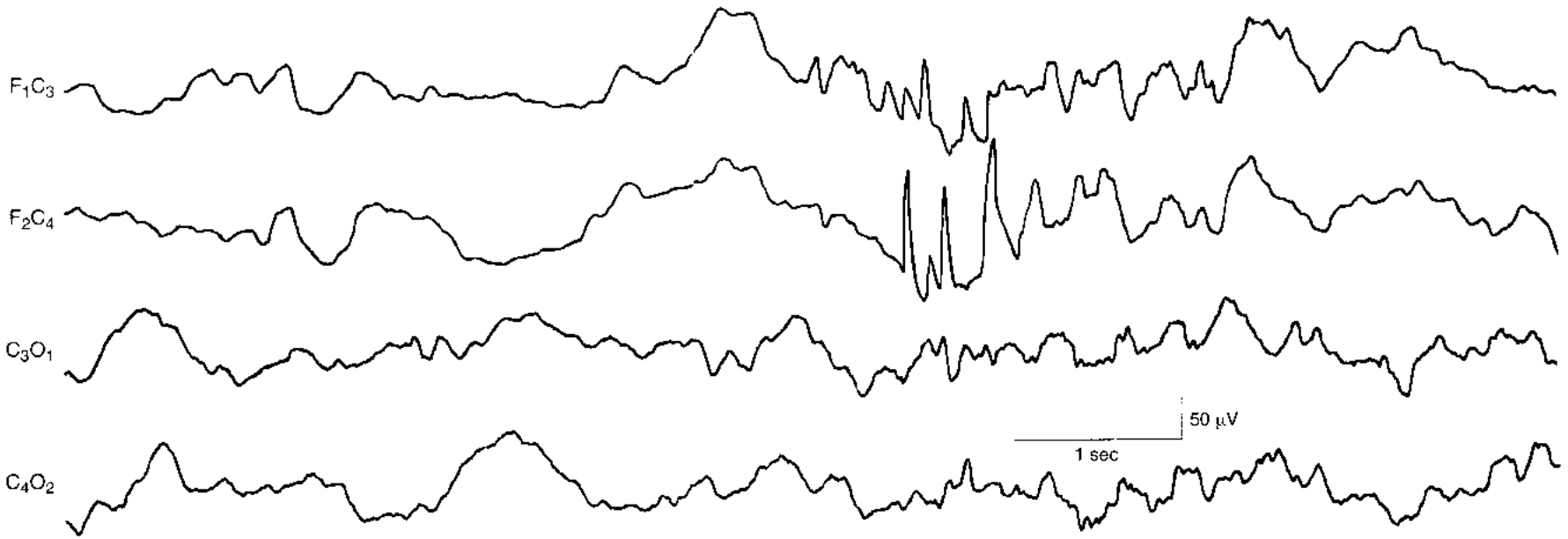


Figure 6.46 Burst of abnormal frontal sharp waves. There is a burst of abnormal sharp waves in the right frontal region in this term infant. This is a selected sample from a 12-channel EEG. (Hrachovy et al., 1990, with permission.)

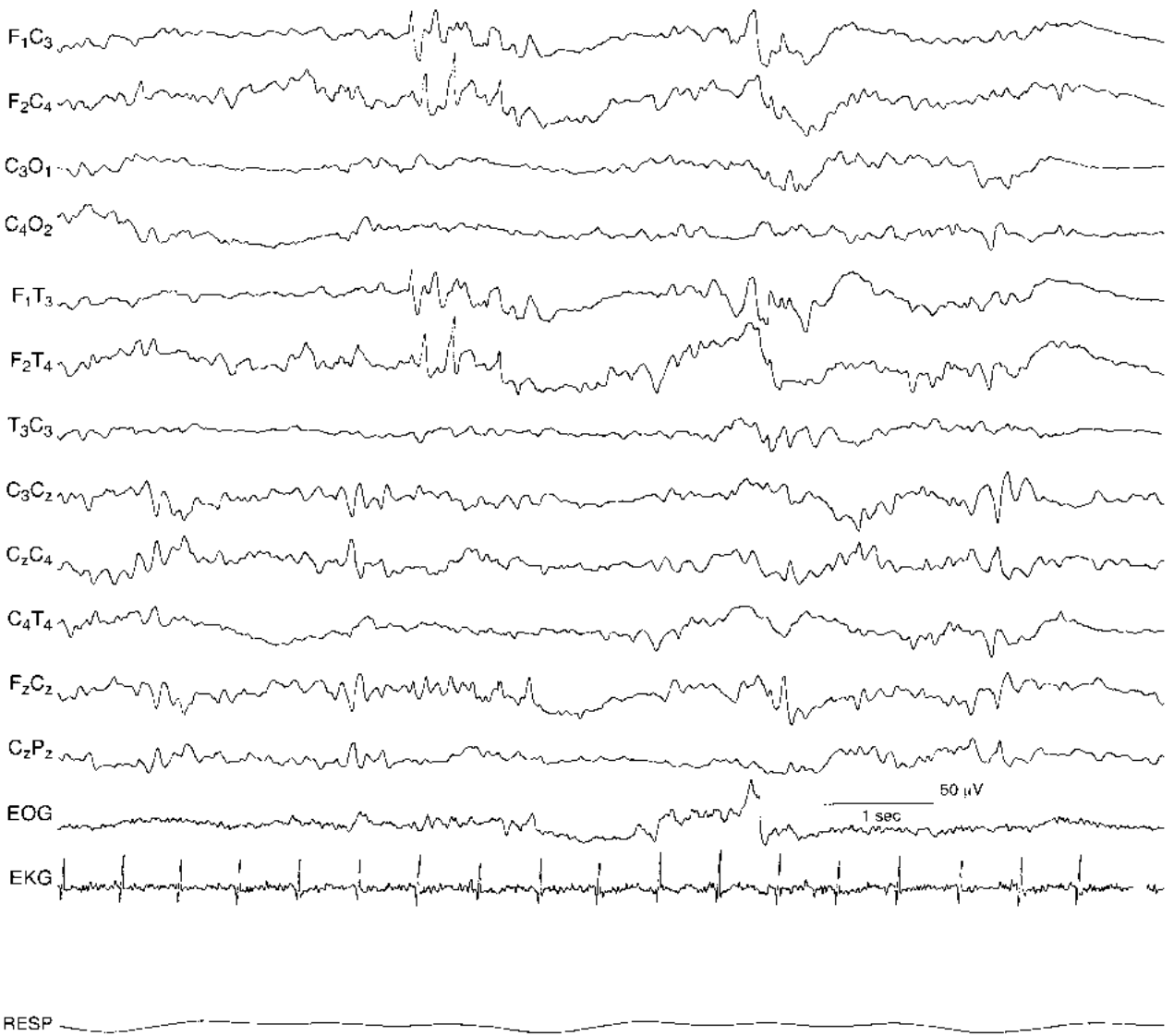


Figure 6.47 Independent bilateral abnormal frontal sharp waves. There are abnormal frontal sharp waves in the first half of this sample. Frontal sharp transients—an expected developmental milestone in this epoch—are present in the second half of the sample, although abnormal because of their asymmetry. In addition, the background EEG activity is undifferentiated in this 40-week CA infant with lactic acidosis and pulmonary insufficiency.

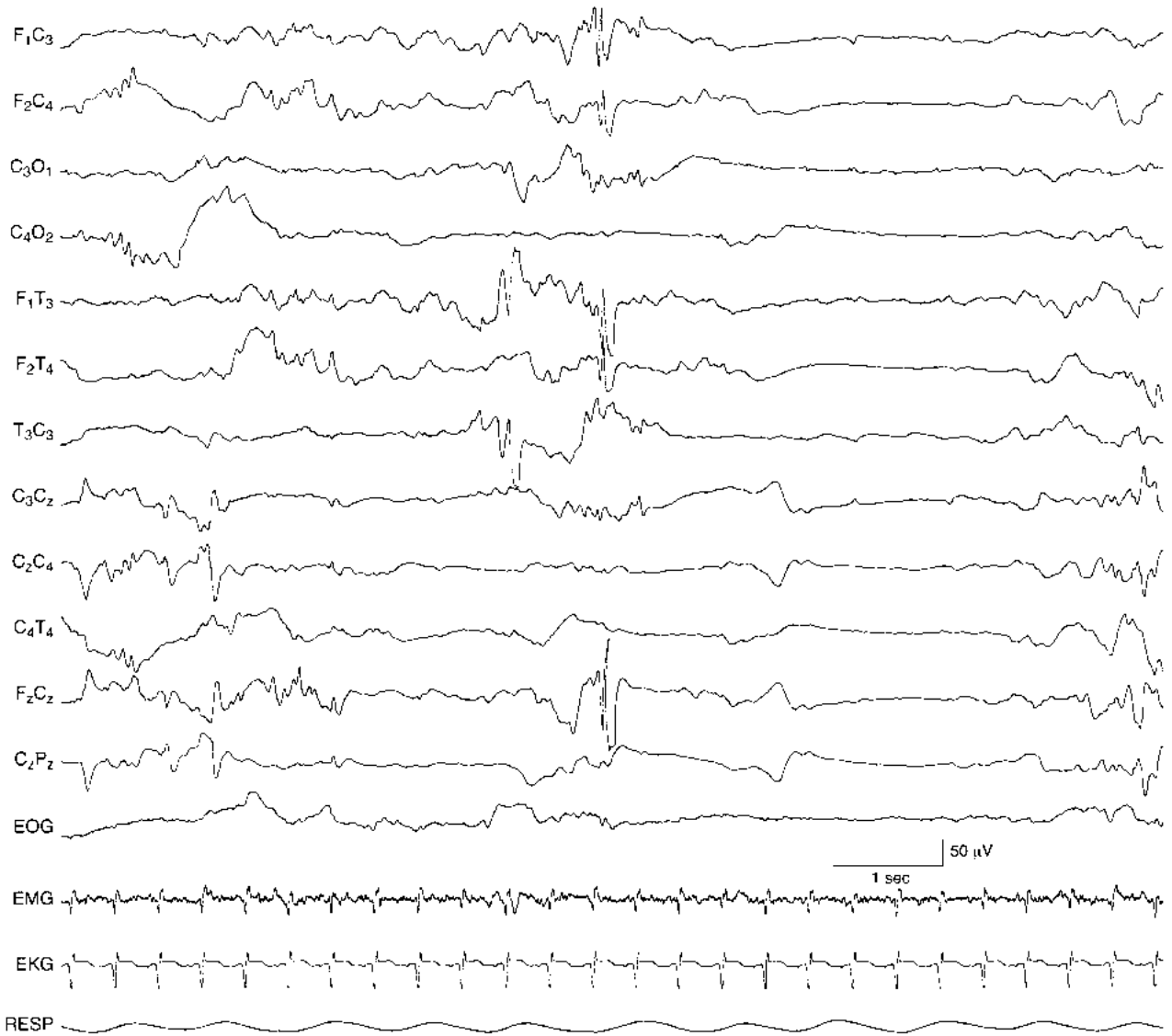


Figure 6.48 Bilateral frontal spikes. There are high-voltage spikes in the frontal regions bilaterally, higher in amplitude on the left, and well-expressed in the midline central region. There is also a temporal sharp wave on the left that occurs earlier. The background EEG activity is discontinuous in this 38-week CA infant with cerebral dysgenesis, congenital ventriculomegaly, and choroid plexus hemorrhage.

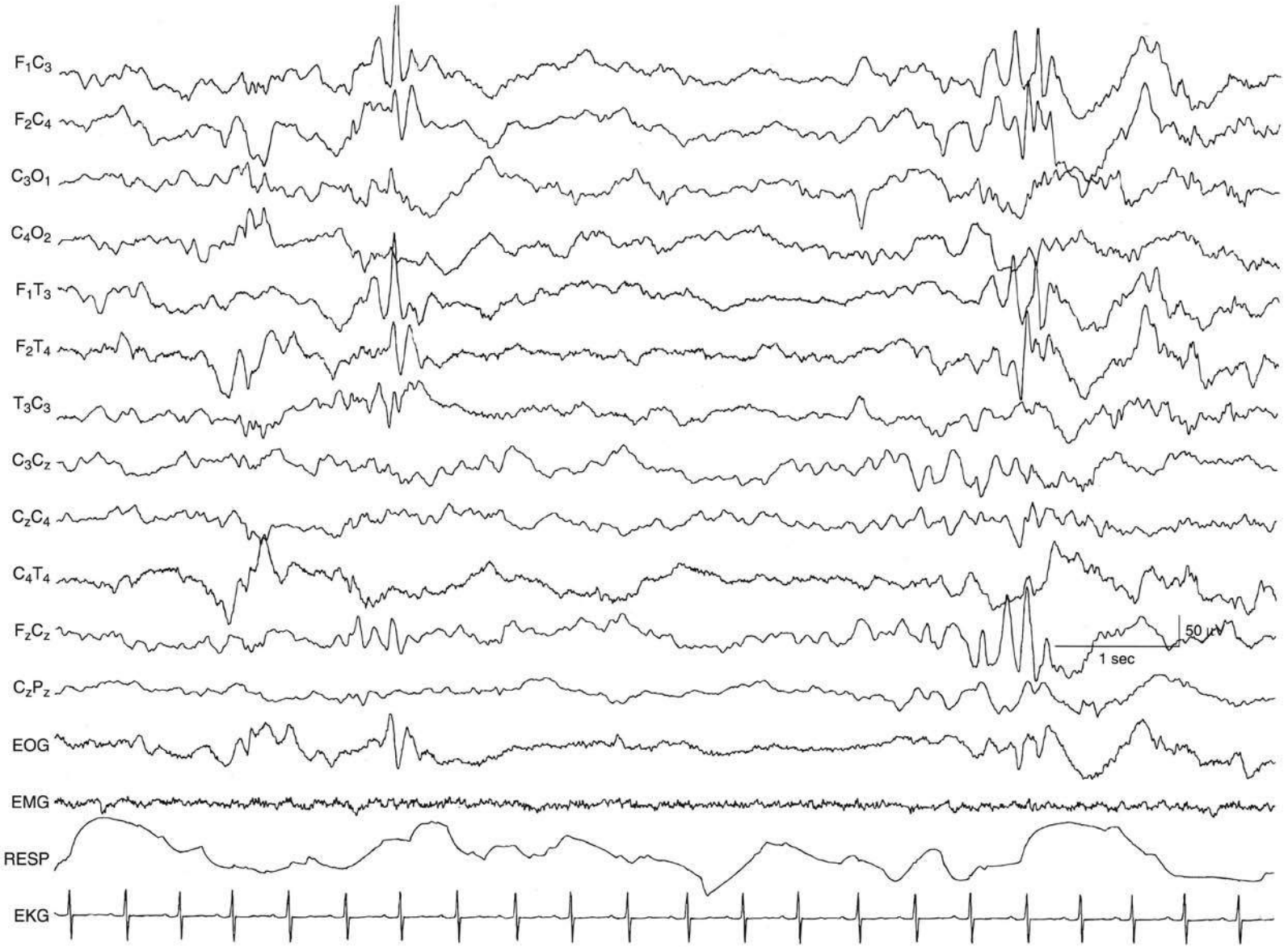


Figure 6.49 Bilateral frontal sharp waves. There are intermittently occurring high-voltage sharp waves in the frontal regions bilaterally. The background EEG activity is within the range of normal variation in this 42-week CA infant suspected of seizures, but without clinical or electrical seizures documented by prolonged EEG.

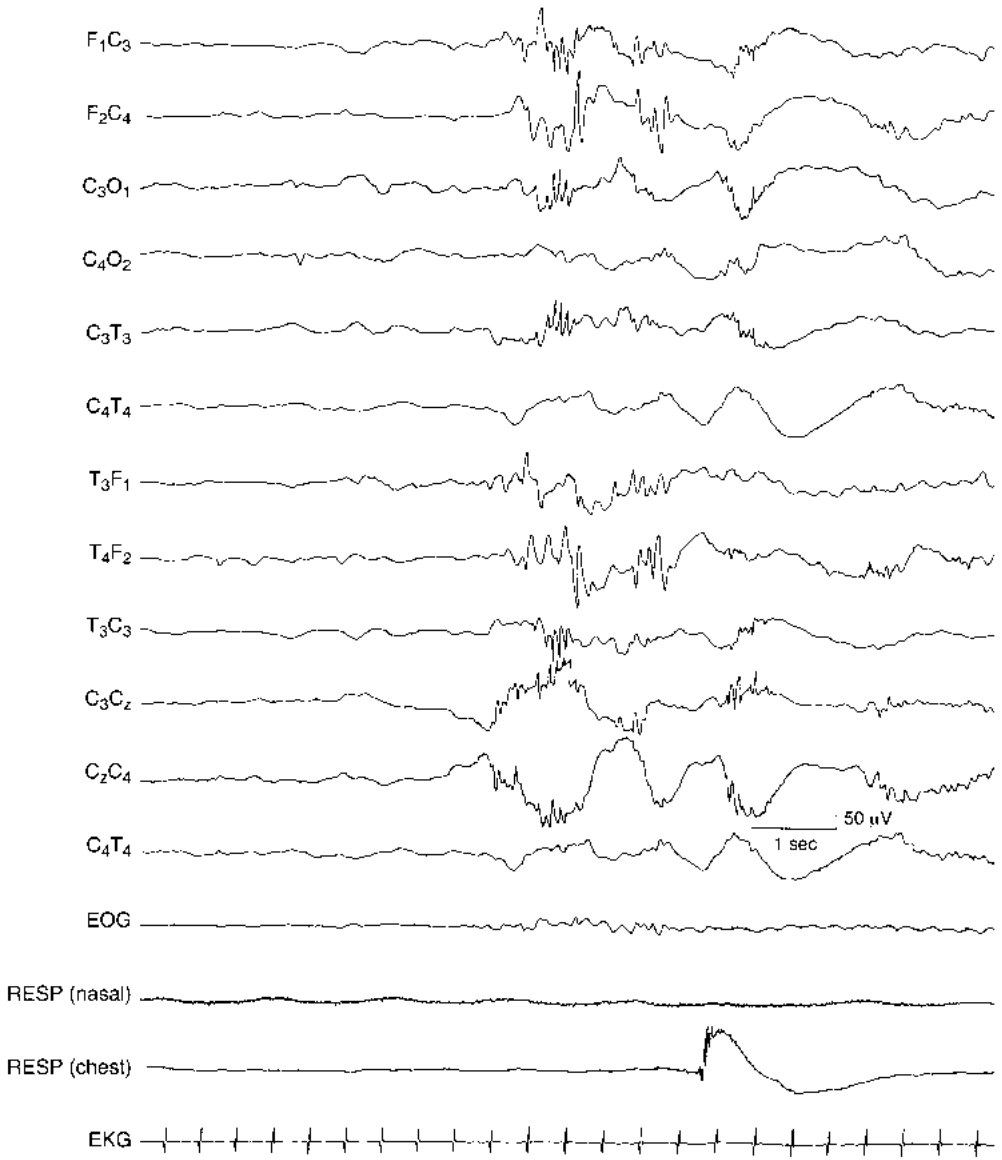


Figure 6.50 Frontal sharp waves and independent central spikes. There are high-voltage sharp waves in the right frontal region and there are runs of low-voltage spikes in the left central region in this 32-week CA age infant.

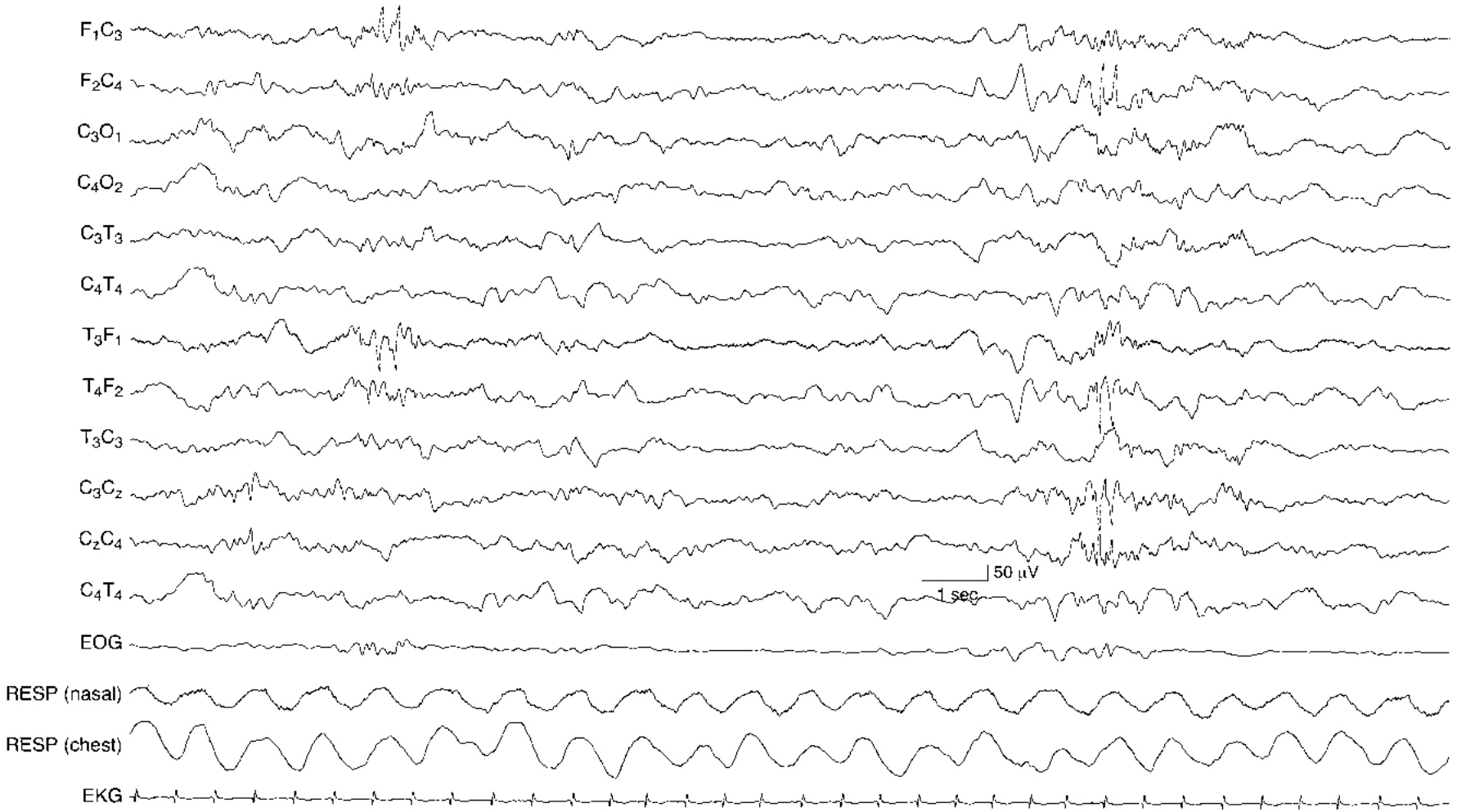


Figure 6.51 Midline and lateralized frontal spikes and sharp waves. There are abnormal sharp waves in the left frontal region and, later in the sample, there are spikes in the right frontal region with expression in the midline central region in this term infant.

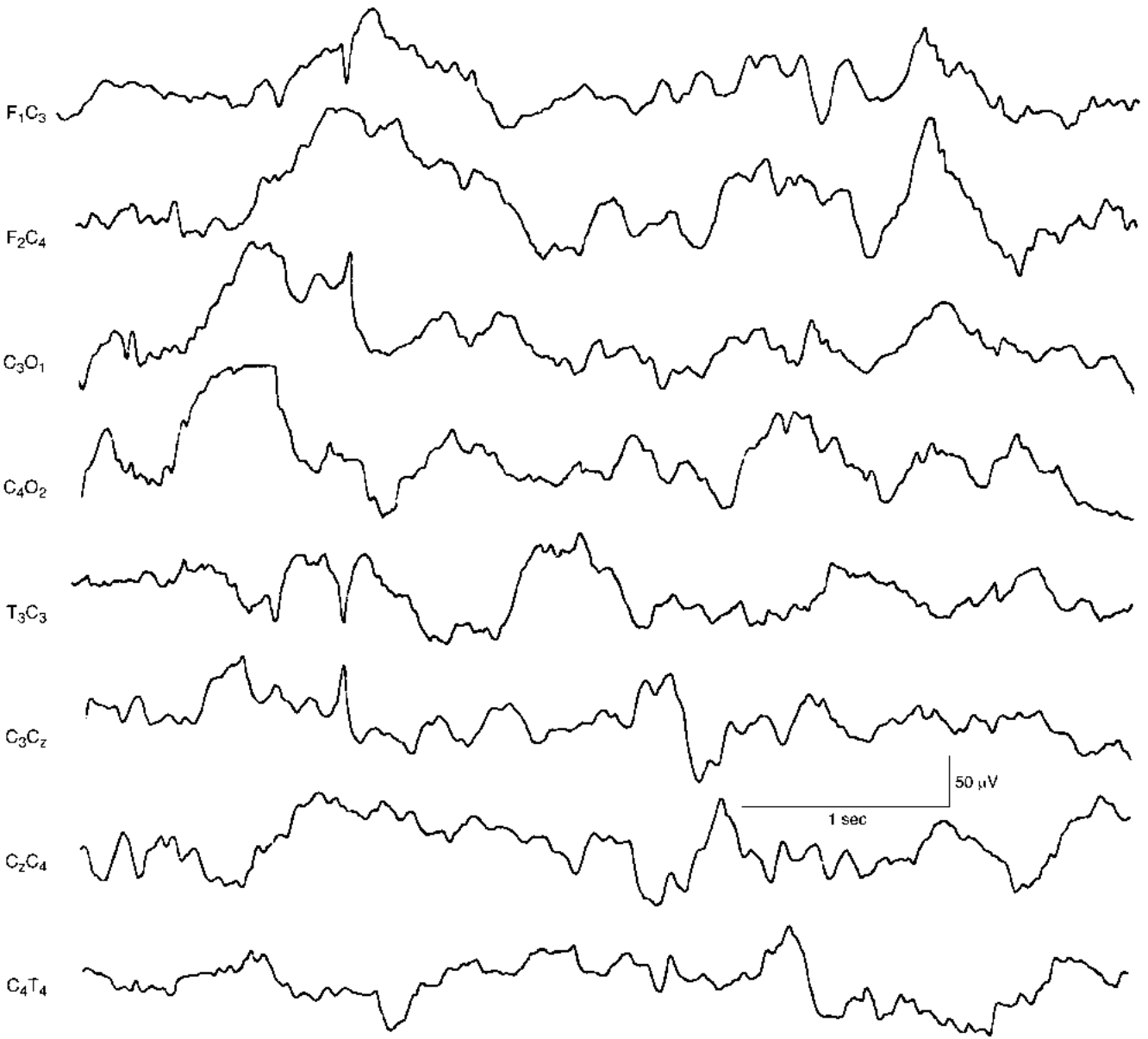


Figure 6.52 Central rapid spikes. There is a single spike discharge in the left central region and normal background EEG activity in this term infant. This sample is taken from a 12-channel EEG recording.

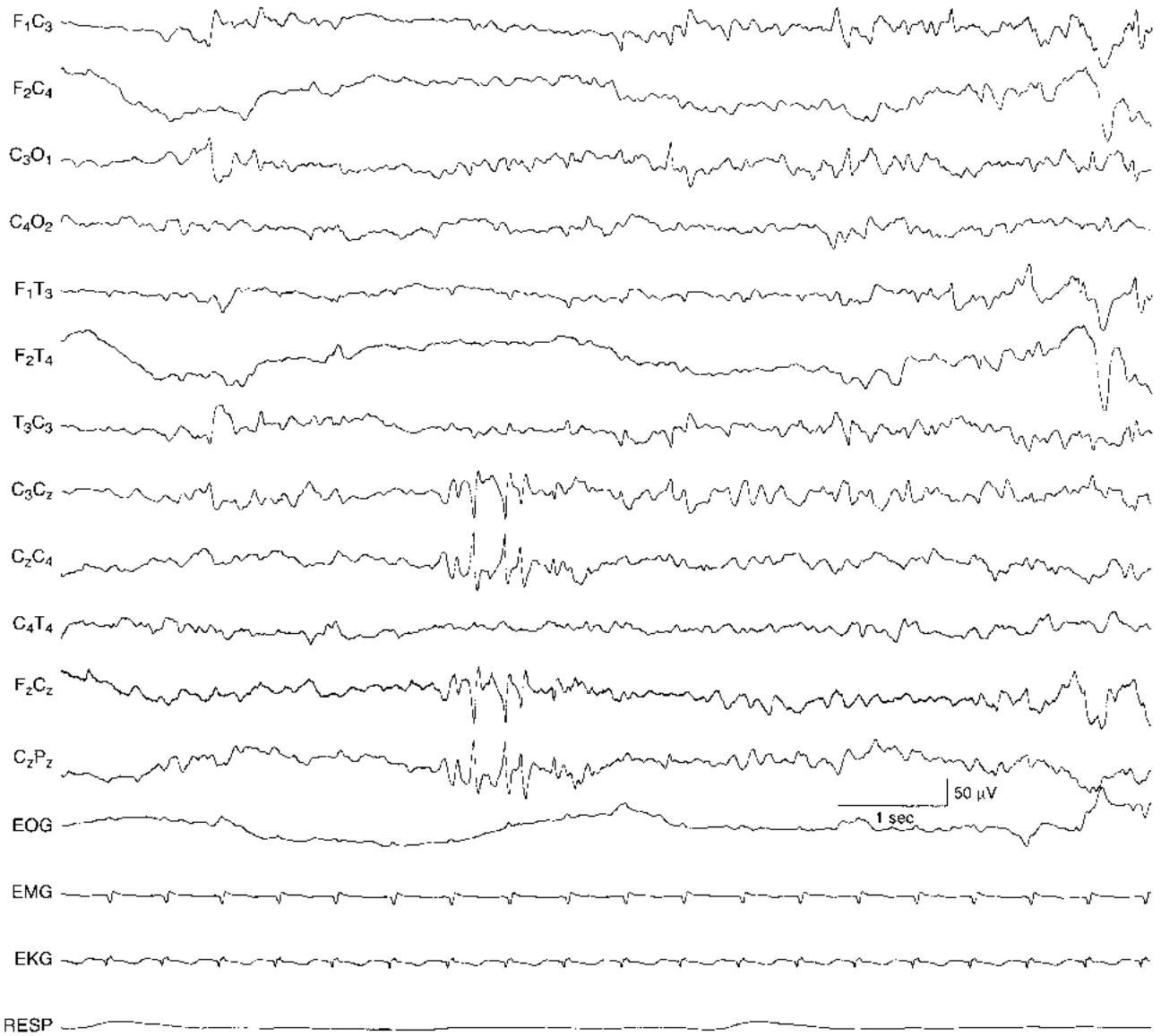


Figure 6.53 Repetitive midline central spikes. There is a run of spikes in the midline central region, expressed in the Cz electrode. The background EEG activity in this 38-week CA infant with cardiac failure and grade I IVH.

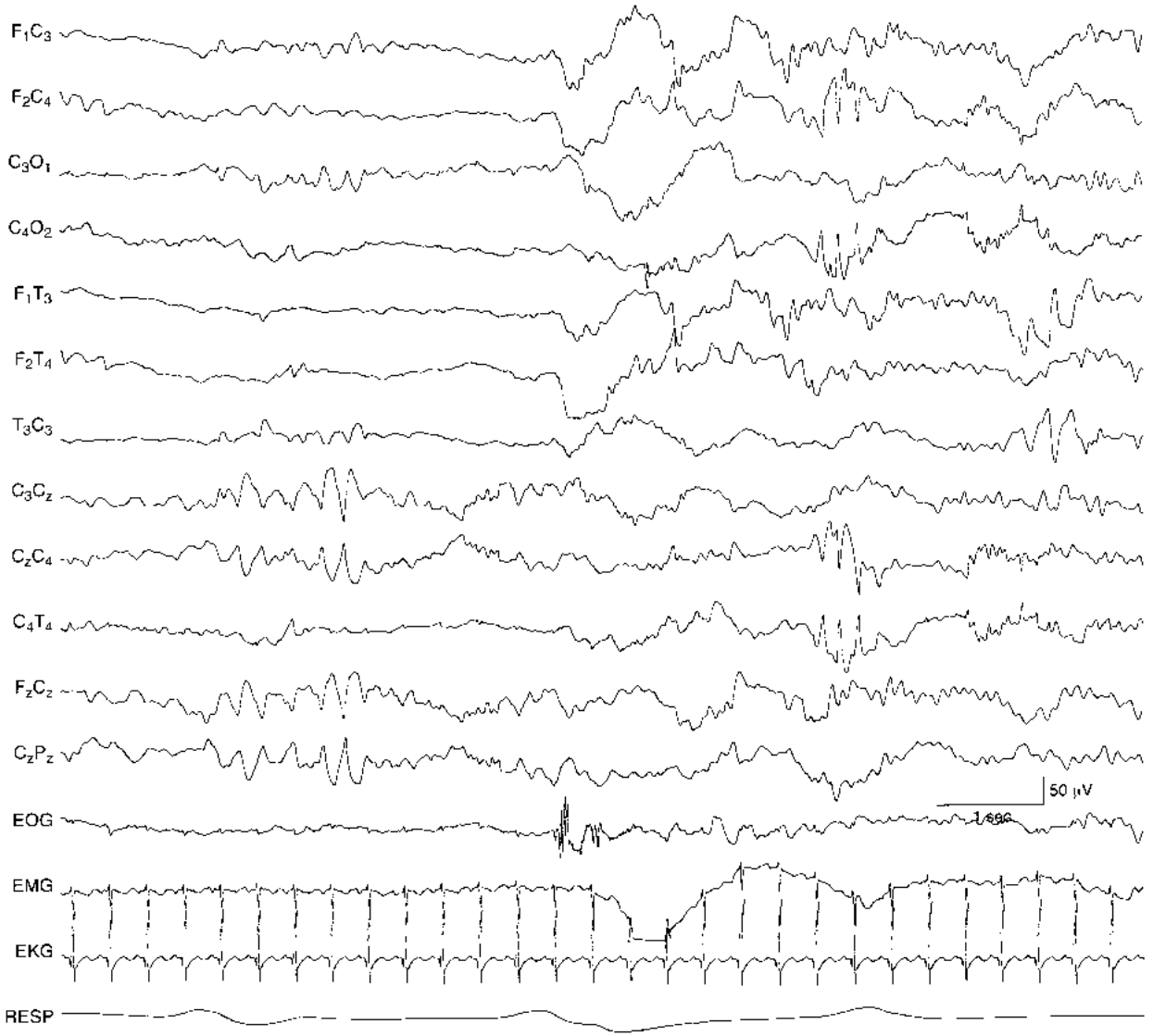


Figure 6.54 Central midline, rhythmic theta, and lateralized central spikes. In the early portion of the recording, there is rhythmic theta activity in the midline central region. Later, there is a run of rhythmic spikes in the right central region. The infant was born at 28-weeks gestational age and at the time of EEG recording was 35 weeks CA. An acute grade III IVH at the time of EEG recording was resolving, although posthemorrhagic hydrocephalus and a porencephalic cyst extended into the left frontal ventricular horn.

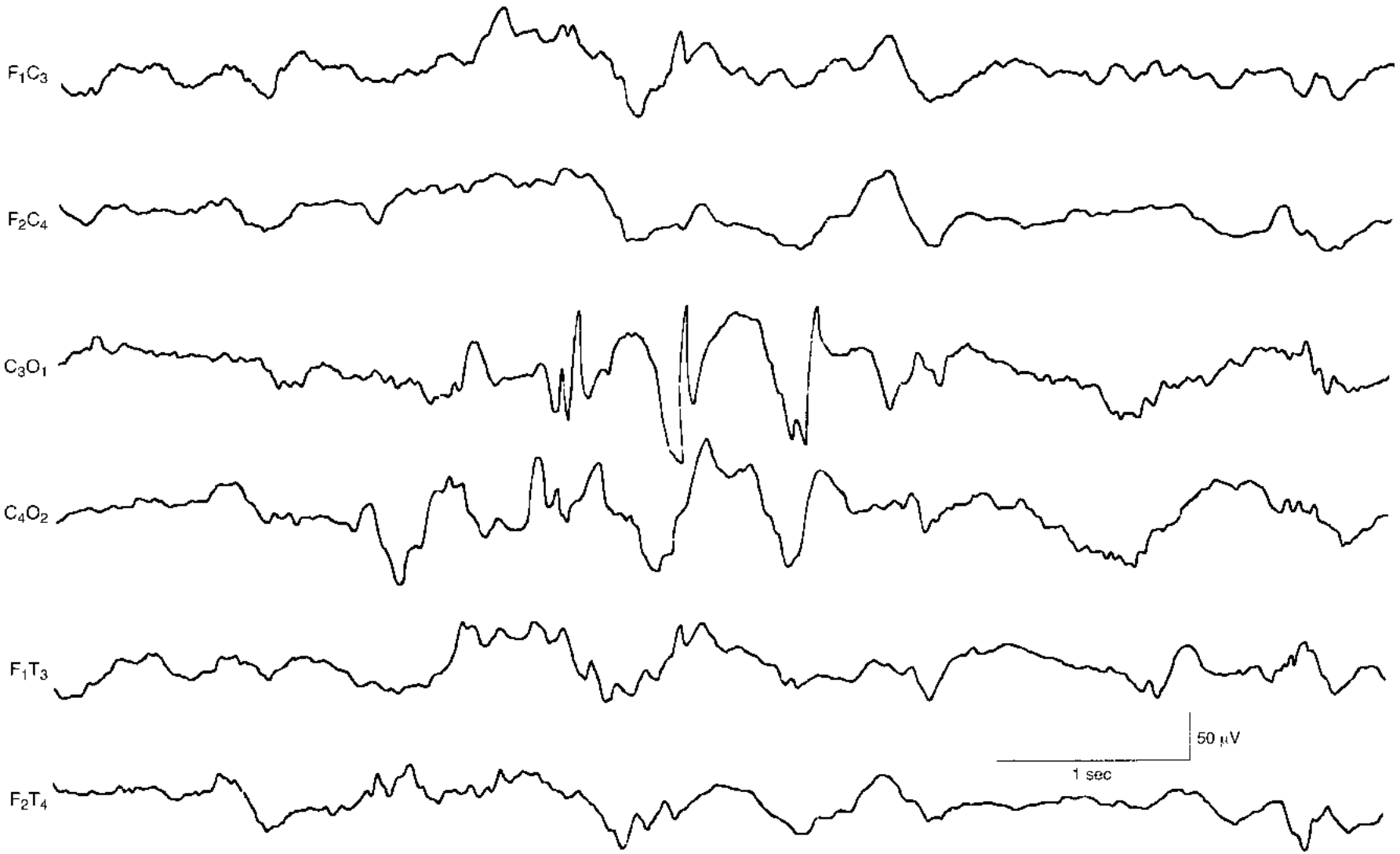


Figure 6.55 Occipital spike and slow waves. There are spike and slow waves in the left occipital region, with some reflection of the slow-wave component on the right. The background EEG activity is within the range of normal variation in this term infant. This sample is selected from a 12-channel EEG.

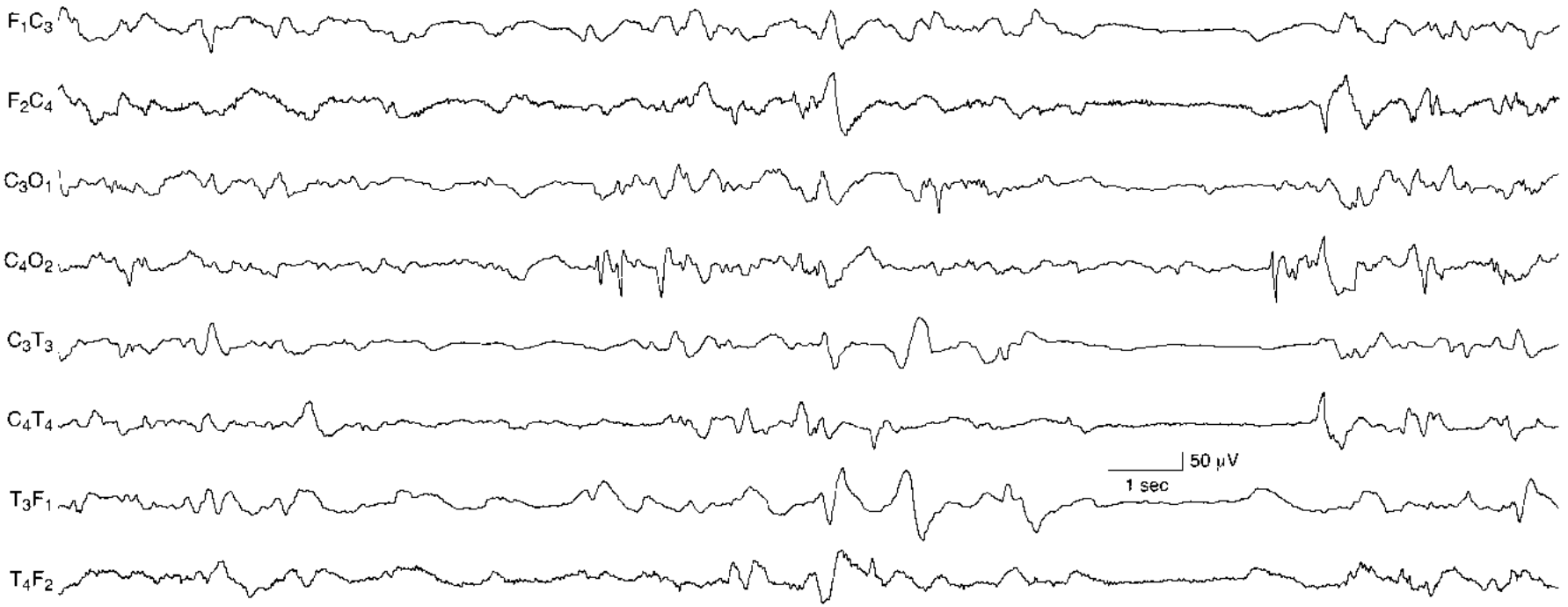


Figure 6.56 Occipital spikes and independent temporal and central sharp waves. There are recurrent spikes in the right occipital region in the mid-portion of this sample. Immediately following this burst, there are frontal sharp transients—normal phenomena. There are also slow temporal sharp waves on the left and independent sharp waves on the right.

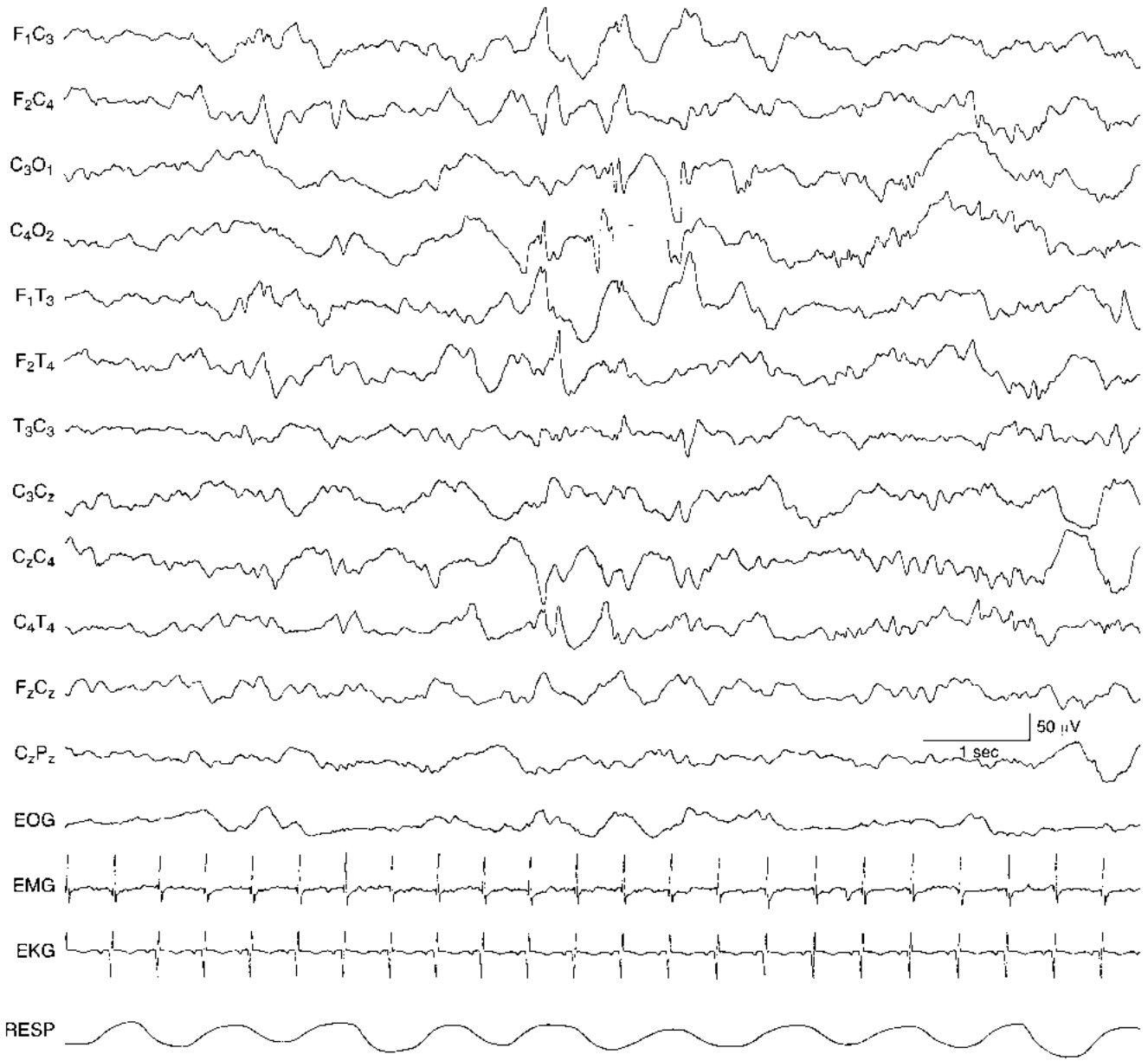


Figure 6.57 Bilateral, independent occipital spikes. There are spike and slow-wave complexes independently in the left and right occipital regions in this 40-week CA infant with Zellweger syndrome.

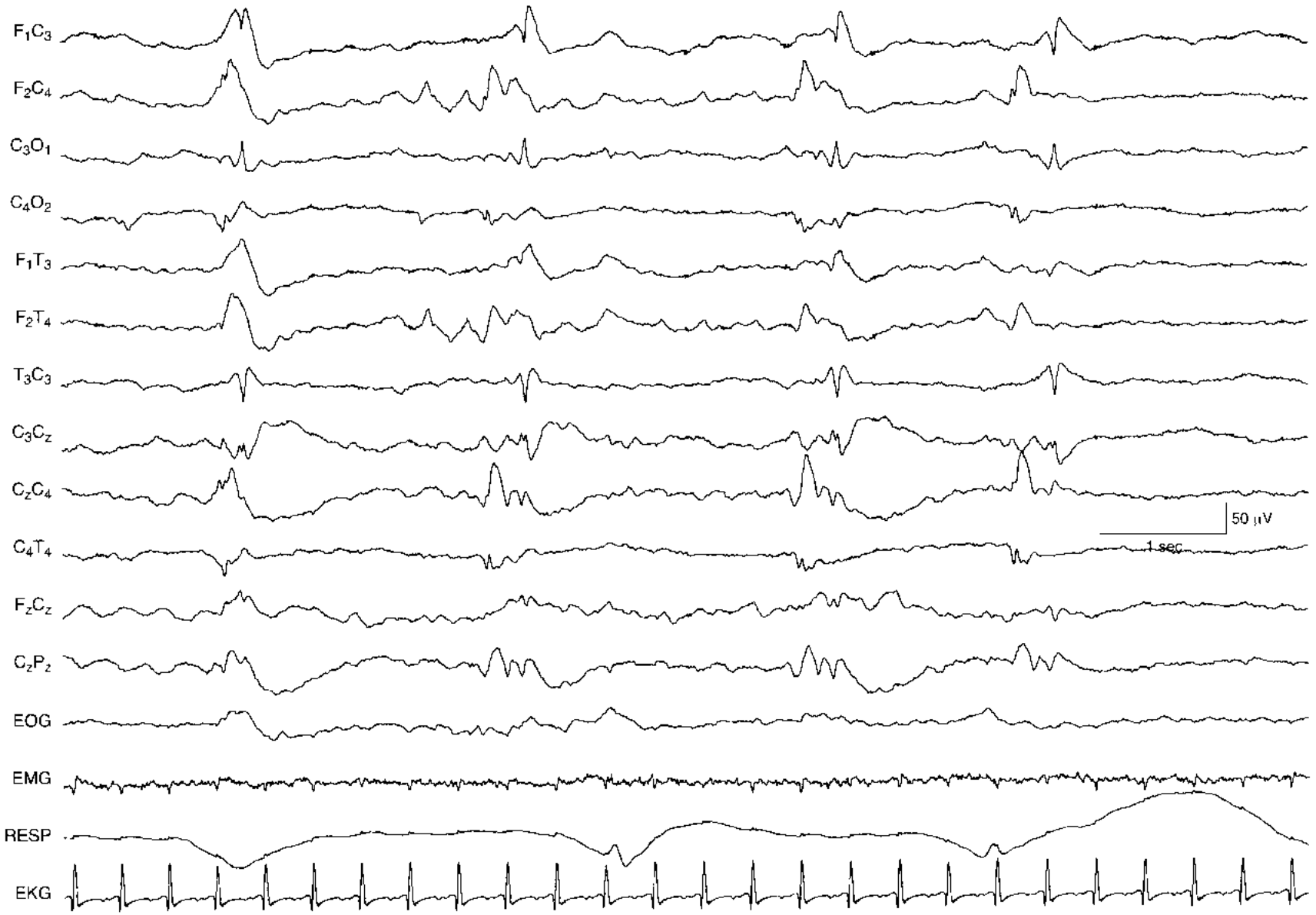


Figure 6.58 Multifocal sharp waves. There are sharp waves, with varying morphology, appearing independently in the left and right central regions in a semiperiodic manner. The background activity is depressed and undifferentiated in this 44-week CA infant with the inborn error of metabolism ornithine carbamylase transferase deficiency.

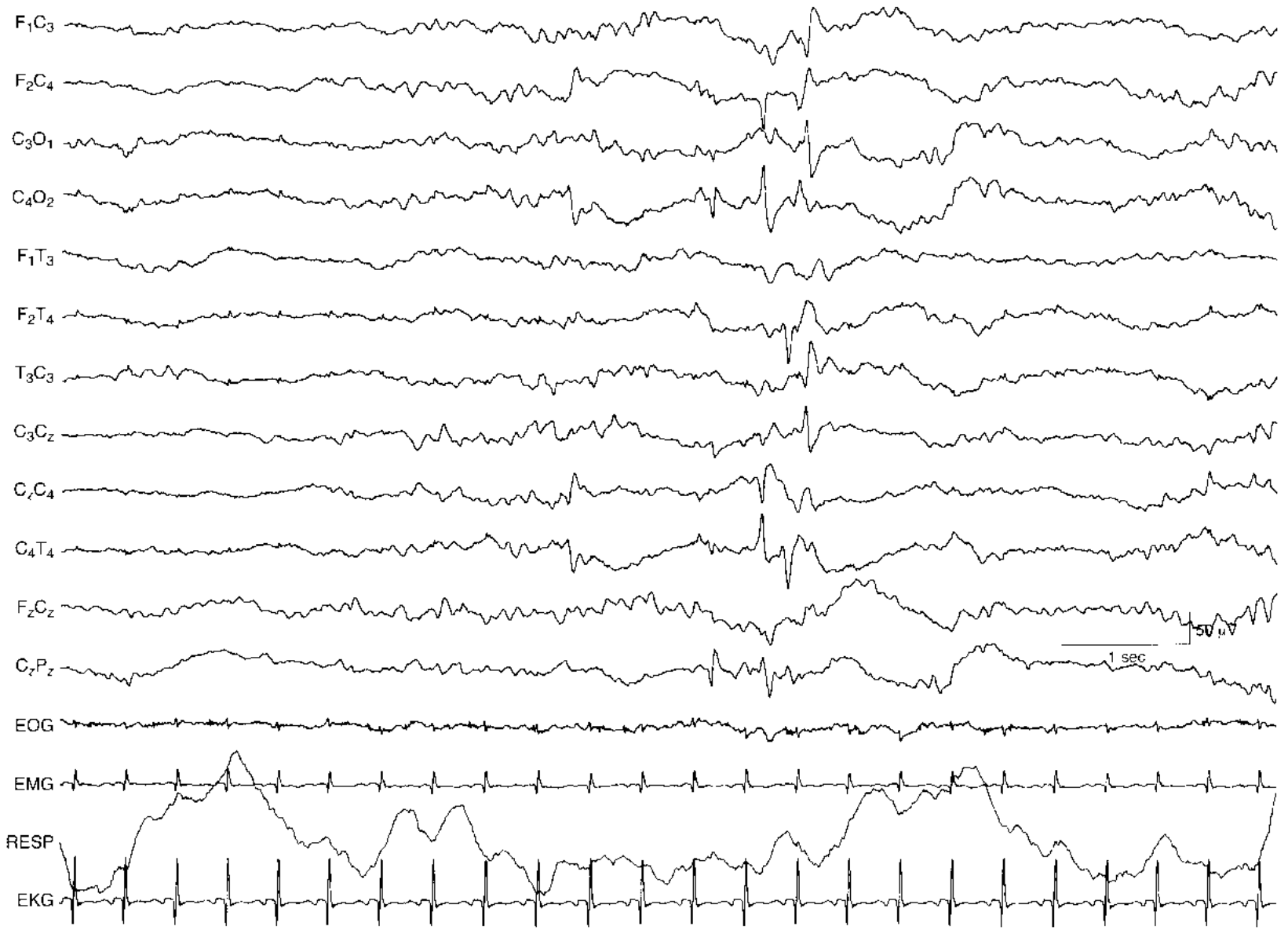


Figure 6.59 Multifocal spikes and sharp waves. There are spikes and sharp waves appearing independently in the left and right central and right temporal regions. The background EEG activity is undifferentiated in this 40-week CA infant with congenital heart disease.

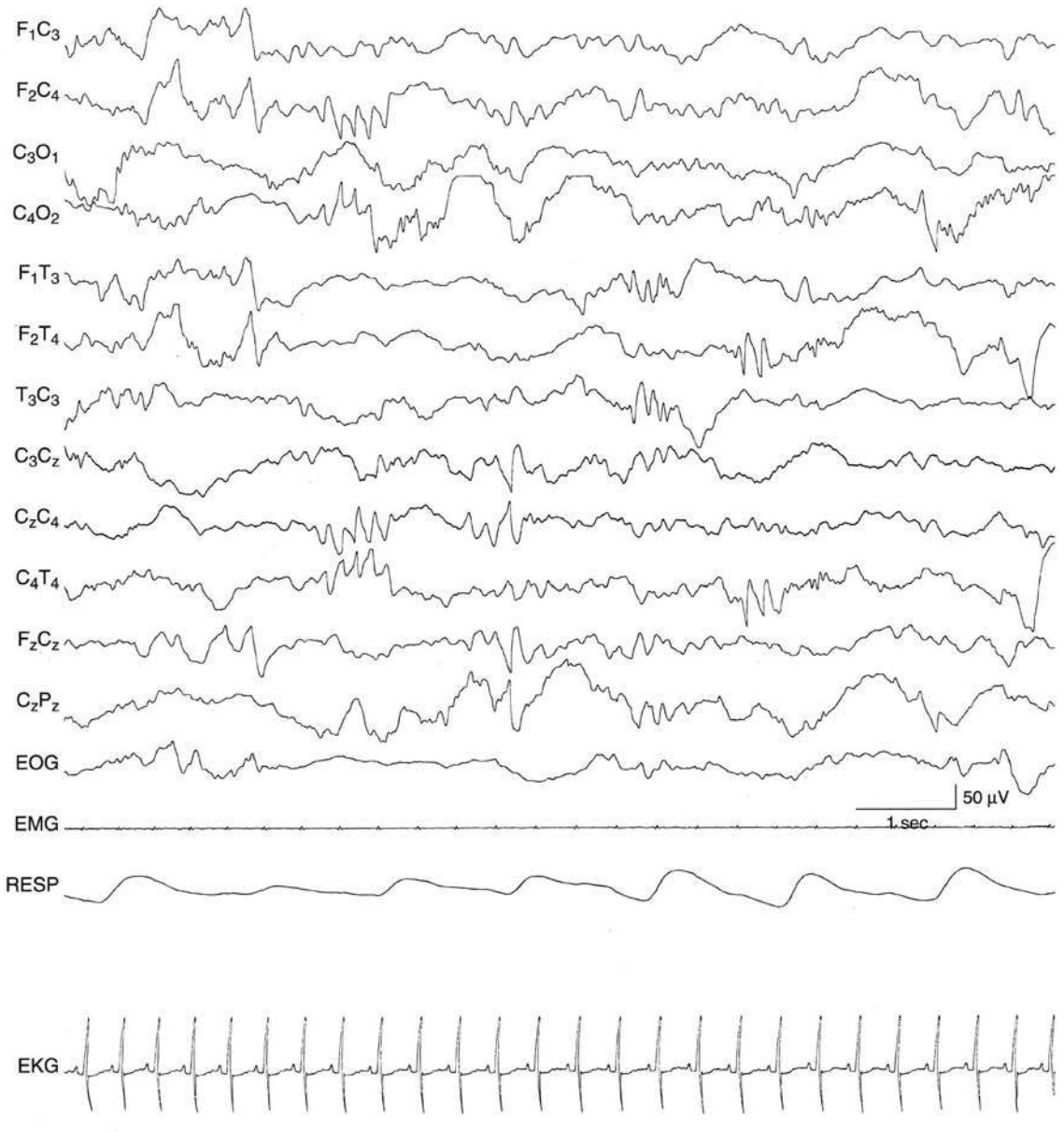


Figure 6.60 Multifocal sharp waves with rhythmic morphology. There are very brief bursts of rhythmic sharp theta activity appearing independently in the left central and left and right temporal regions. The background activity is undifferentiated in this infant with HSVE.

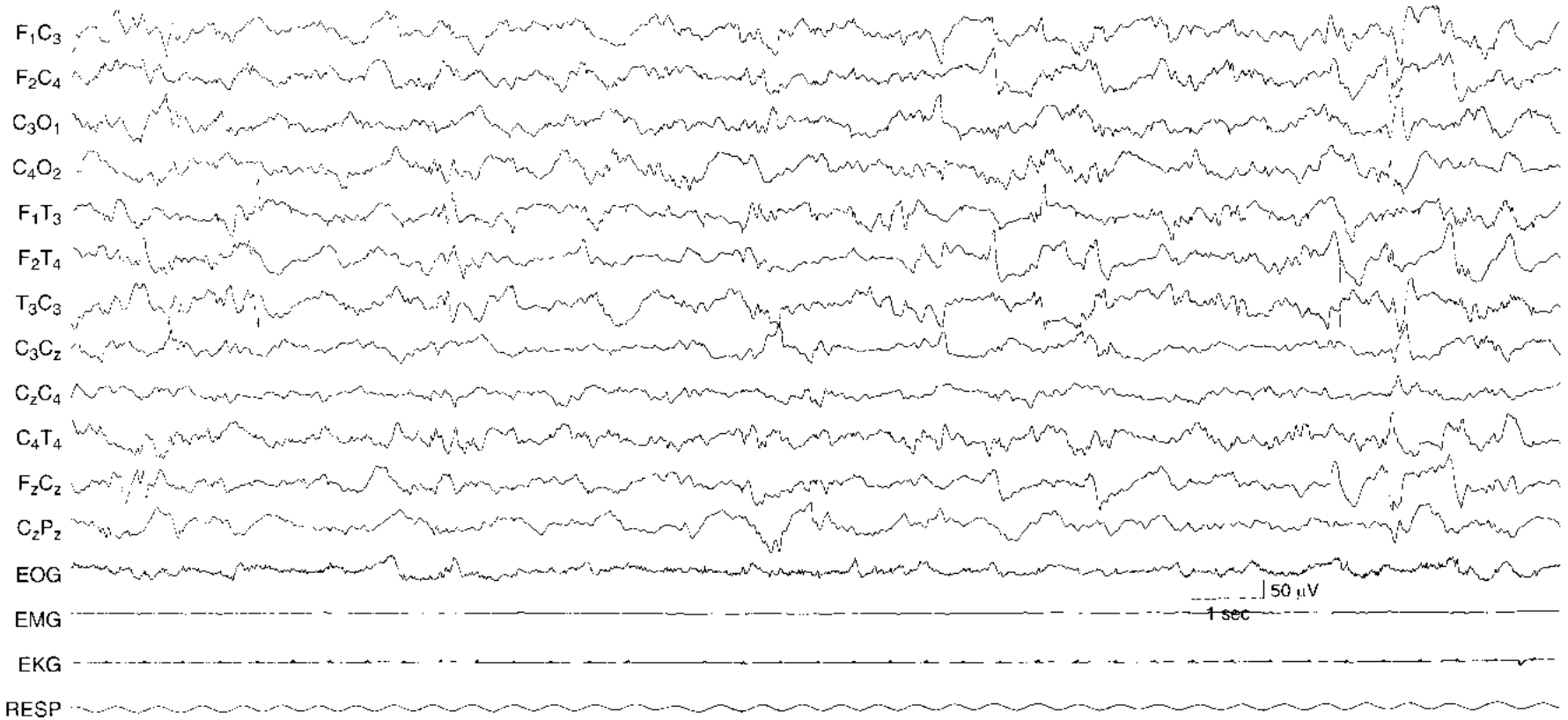


Figure 6.61 Surface positive and surface negative multifocal sharp waves. There are sharp waves present in the left and right central and left and right temporal regions. Some of the waveforms are surface positive (left temporal early in the sample) and others are surface negative in this term infant with renal failure.

CHAPTER 7

Neonatal Seizures

The electrographic and clinical characteristics of seizures in the neonate are unique compared to older children and adults. In the neonate, interictal epileptiform discharges are rarely present to aid in diagnosis, electrographic seizure patterns vary widely, electrical seizure activity does not accompany all behaviors currently considered to be seizures, and electrical seizure activity may occur without evident clinical seizures (Kellaway and Hrachovy, 1983; Mizrahi and Kellaway, 1987, 1998).

This chapter addresses the electroencephalographic (EEG) and clinical features of neonatal seizures. Other pertinent issues concerning neonatal seizures that relate to epileptogenesis of the immature brain, the effect of seizures on the developing brain, pathophysiology, etiology, therapy, and prognosis are beyond the scope of an atlas of neonatal electroencephalography, but are considered in detail elsewhere (Bye et al., 1997; Clancy, 1996; Ellenberg et al., 1984; Glass, 2014; Hellstrom et al., 2015; Holmes, 2002; Holmes 2009; Holmes et al., 2002; Lombroso, 1996a, 1996b; McBride et al., 2000; Mizrahi, 1999, 2001; Mizrahi and Clancy, 2000; Mizrahi and Kellaway, 1998; Mizrahi and Watanabe, 2002; Ortibus et al., 1996; Painter et al., 1999; Rennie, 1997; Scher, 1997, 2002; Stafstrom and Holmes, 2002; Swann, 2002; Swann and Hablitz, 2000; Tharp, 2002; Velisek and Moshe, 2002; Watanabe, 2014).

In considering neonatal seizures, important features of interpretation include recognition of EEG seizures and the determination of the significance of focal sharp waves that may occur between seizures. Electrical seizure activity in the newborn has some features similar to those of older children and adults, but also several features are characteristic of the neonate. These are discussed later. As previously discussed in Chapters 4 through 6, focal sharp waves in the neonatal EEG may be normal, of uncertain diagnostic significance, or abnormal. However, they generally do not correlate with the presence of epileptic seizures. Thus, the finding of isolated sharp waves in an infant suspected of seizures does not provide evidence that a seizure has occurred or will occur.

In addition, the correlation of electrical seizure activity with the occurrence of clinical seizures is critical. This is most effectively accomplished by direct observation at the bedside during EEG recording or by EEG-video monitoring. When the clinical behaviors in question are not witnessed directly or recorded on video, the neurophysiologist must rely on the description of the clinical event through notations made by the electroneurodiagnostic technologist (ENDT) at the time of recording.

CLINICAL CHARACTERISTICS OF NEONATAL SEIZURES

The occurrence of clinical seizures may often be the first, and sometimes the only, manifestation of central nervous system (CNS) dysfunction in the neonate. As such seizure occurrence represents an emergent problem since some causes of seizures can be successfully treated, with the potential to limit associated brain injury. Direct or indirect alterations may occur in respiration, heart rate, or systemic blood pressure in association with clinical seizures or with their aggressive therapy. While data suggest that the immature brain may be more resistant to seizure-induced injury than the mature brain (Albala et al., 1984; Sperber et al., 1991; Stafstrom et al., 1992; Thurber et al., 1994), recent data suggest that there may be both short-term and long-term consequences of seizures in the developing brain (Cilio et al., 2003; de Rogalski et al., 2001; Holmes and Ben-Ari, 2002; Holmes et al., 2002; Villeneuve et al., 2000).

The concepts of which motor and autonomic phenomena constitute clinical seizures have continually changed over the years (Burke, 1954; Cadilhac

et al., 1959; Dreyfus-Brisac and Monod, 1964; Fenichel et al., 1979; Harris and Tizard, 1960; Hrachovy and Kellaway, 1983; Minkowski et al., 1955; Mizrahi and Kellaway, 1987; Perlman and Volpe, 1983; Rose and Lombroso, 1970; Volpe, 1973; Watanabe et al., 1977). More recently, there has been greater consensus. All of the clinical behaviors currently considered as neonatal seizures have been recorded and analyzed, utilizing EEG/polygraphic/video monitoring in studies of characterization as well as seizure surveillance (Andropoulos et al., 2010; Biagioni, et al., 1998; Boylan et al., 2013; Bye and Flanagan, 1995; Clancy et al., 2005; Mizrahi and Kellaway, 1987; Plouin, 2000; Scher et al., 1993; Pressler and Mangum, 2013; Pisani et al., 2008; Nagarajan et al., 2011a). Some behaviors are not consistently accompanied by electrical seizure activity, and many behaviors consistently occurred without ictal discharges (Mizrahi and Kellaway, 1987). Despite this variable relationship of clinical seizures to electrical seizure activity, all clinical seizures occurred in association with CNS disorders. These findings indicate that different types of neonatal seizures may reflect different pathophysiological mechanisms—epileptic or nonepileptic and regardless of their pathophysiology and relation to electrical seizure activity, the clinical behaviors known as neonatal seizures reliably indicate the presence of CNS dysfunction (Boylan et al., 1999).

TERMINOLOGY AND CLASSIFICATION

Electroclinical Classification

Although the pathophysiologic mechanisms underlying neonatal seizure may be debated, it is important to develop a working seizure classification system that can be effectively used to identify specific abnormal clinical behaviors associated with CNS disease. Regardless of their pathophysiology, all of the phenomena considered to be seizures are "seizures" in the generic sense, without necessarily implying that they are all epileptic. Eventually it may become evident that some "seizures" are epileptic in origin, whereas others are initiated and elaborated by nonepileptic mechanisms.

A number of approaches are used in the classification of neonatal seizures. A classification system based on clinical features is presented in Table 7.1 along with other clinical signs that may aid in classification and the determination of their presumed pathophysiology (Kellaway and Mizrahi, 1987; Mizrahi and Kellaway, 1987). Table 7.2 lists seizure types, clinical features, electrographic correlates, and presumed pathophysiology. In addition, from the perspective of the neonatal EEG, neonatal seizures can be classified according to the temporal relationship between the electrical event and the clinical event: electroclinical seizures (an overlap in time of electrographic seizures and clinical seizures with close correlation), clinical-only seizures (with no concurrent electrographic seizures), and electrical-only seizures (with no concurrent clinical seizures).

Electroclinical Seizures

Electroclinical seizures are characterized by a temporal overlap between clinical seizures and electrical seizure activity on EEG. In many instances, the electrical seizure and clinical events are closely associated, with the onset and termination of both events coinciding. However, this may not always be the case: Clinical onset may precede electrical onset, electrical onset may precede clinical onset, and either the clinical or electrical seizure may terminate first.

Focal clonic, focal tonic, and some myoclonic seizures and spasms are associated with electrical seizure activity. Some clinical features of focal clonic seizures are unique to this age group. The seizures may be multifocal with alternating, asynchronous, or migrating clonic jerking; hemiconvulsive, involving an entire side of the body; or may appear as clonic jerking of axial musculature of the trunk, abdomen, neck, or tongue. Focal tonic seizures with asymmetrical trunk or limb posturing or tonic eye deviation are also associated with electrical seizure activity. In addition, some focal or generalized myoclonic jerks also are consistently accompanied by EEG seizures discharges. A special, and rare, circumstance is the occurrence of spasms associated with generalized voltage attenuation or generalized slow transients.

Focal clonic seizures may occur in infants who appear to be awake and alert and with an EEG background activity that may be normal. The etiological factors are most often infarction, intracerebral hemorrhage, subarachnoid hemorrhage, and, more rarely, metabolic disorders such as hypoglycemia and hypocalcemia. The short-term outcome of infants with focal clonic seizures is good compared with infants who have other types of seizures based upon the degree and distribution of accompanying brain injury.

Clinical-Only Seizures

Some types of clinical seizures have no specific relation to electrical seizure activity. Those that occur in the absence of any electrical seizure activity include generalized tonic, motor automatisms, and some myoclonic seizures. Generalized posturing may be flexor or extensor or may be mixed extensor/flexor. Motor automatisms include oral-buccal-lingual movements such as lip-smacking, sucking, and tongue protrusion; ocular signs such as roving eye movements, blinking, and nystagmus; progression movements such as pedaling or stepping of legs, or swimming or rotary movements of the arms; and complex purposeless movements such as struggling or thrashing. These clinical events, referred to as "motor automatisms" (Mizrahi and Kellaway, 1987) are equivalent to some described as "little peripheral phenomena"

Table 7.1 Clinical Characteristics, Classification, and Presumed Pathophysiology of Neonatal Seizures

Classification	Characterization
Focal clonic	Repetitive, rhythmic contractions of muscle groups of the limbs, face, or trunk
	May be unifocal or multifocal
	May occur synchronously or asynchronously in muscle groups on one side of the body
	May occur simultaneously, but asynchronously on both sides
	Cannot be suppressed by restraint
	Pathophysiology: epileptic
Focal tonic	Sustained posturing of single limbs
	Sustained asymmetrical posturing of the trunk
	Sustained eye deviation
	Cannot be provoked by stimulation or suppressed by restraint
	Pathophysiology: epileptic
Generalized tonic	Sustained symmetrical posturing of limbs, trunk, and neck
	May be flexor, extensor, or mixed extensor/flexor
	May be provoked or intensified by stimulation
	May be suppressed by restraint or repositioning
	Presumed pathophysiology: nonepileptic
Myoclonic	Random, single, rapid contractions of muscle groups of the limbs, face, or trunk
	Typically not repetitive or may recur at a slow rate
	May be generalized, focal, or fragmentary
	May be provoked by stimulation
	Presumed pathophysiology: may be epileptic or nonepileptic
Spasms	May be flexor, extensor, or mixed extensor/flexor
	May occur in clusters
	Cannot be provoked by stimulation or suppressed by restraint
	Pathophysiology: epileptic
Motor automatisms **Ocular signs**	Random and roving eye movements or nystagmus (distinct from tonic eye deviation)
	May be provoked or intensified by tactile stimulation
	Presumed pathophysiology: nonepileptic

(*Continued*)

Table 7.1 Clinical Characteristics, Classification, and Presumed Pathophysiology of Neonatal Seizures (*Continued*)

Classification	Characterization
Oral-buccal-lingual movements	Sucking, chewing, tongue protrusions
	May be provoked or intensified by stimulation
	Presumed pathophysiology: nonepileptic
Progression movements	Rowing or swimming movements
	Pedaling or bicycling movements of the legs
	May be provoked or intensified by stimulation
	May be suppressed by restraint or repositioning
	Presumed pathophysiology: nonepileptic
Complex purposeless movements	Sudden arousal with transient increased random activity of limbs
	May be provoked or intensified by stimulation
	Presumed pathophysiology: nonepileptic

Dreyfus-Brisac and Monod (1964), as "subtle seizures" by Volpe (1973), and as "minimal seizures" by Lombroso (1974). Myoclonic jerks may also be present without accompanying EEG seizure discharges. They may be generalized, or they may be confined to limited muscle groups.

Tonic posturing, motor automatisms, and myoclonic jerks most often occur in infants who are lethargic or obtunded. The EEG background activity is typically depressed and undifferentiated. The etiology of these seizure types is most often hypoxic-ischemic encephalopathy. Compared with focal clonic seizures, clinical seizures without electrical seizure activity are more often associated with a poorer prognosis with high morbidity and mortality.

Electrical Seizure Activity Without Evident Clinical Seizures

Subclinical electrical seizure activity—that is, electrical seizure activity with no clinical accompaniment (Clancy et al., 1988; Mizrahi and Kellaway, 1987)—occurs in several situations. This may occur in an infant who is pharmacologically paralyzed for respiratory care. Typically, no behavioral changes are associated with seizure discharges of the depressed brain or alpha seizures discharges (see later). Third, antiepileptic drugs (AEDs) may suppress the clinical component of the electroclinical seizure but not the electrical component: The clinical seizure may be controlled but electrical seizure activity may persist.

Additional Issues of Classification

Seizures With Autonomic Nervous System Features

It has been reported that some clinical seizures consist predominantly of changes in respiration, blood pressure, or heart rate; pupillary constriction or dilatation; pallor or flushing; or drooling or salivation (Mizrahi and Kellaway, 1998). The relation of these paroxysmal autonomic events to electrical seizure activity or the frequency of their occurrence as ictal phenomena have not been firmly established. For example, apnea can occur as an ictal event with associated electrical seizure activity, but this is rare compared with other causes of apnea in newborns. If apnea occurs in close relation to an EEG seizure discharge, it is likely to be accompanied by other motor or behavioral seizure phenomena. Thus, autonomic features more likely occur as components of clinical seizures with motor manifestations than as the sole manifestation of a clinical seizure.

Mixed Seizure Types

Several types of clinical seizures may occur in the same patient: electroclinical, clinical only, and electrical only. For example, an infant with tonic posturing unassociated with electrical seizure activity may also exhibit focal clonic seizures that have a distinct electrical signature. In addition, electrical seizure activity may occur without behavioral correlates in infants who at other times have clinical seizures either with or without electrical seizure discharges.

Table 7.2 Classification of Neonatal Seizures Based Upon Electroclinical Findings

CLINICAL SEIZURES WITH A CONSISTENT ELECTROCORTICAL SIGNATURE (*PATHOPHYSIOLOGY: EPILEPTIC*)
Focal clonic
Unifocal
Multifocal
Hemiconvulsive
Axial
Focal tonic
Asymmetrical truncal posturing
Limb posturing
Sustained eye deviation
Myoclonic
Generalized
Focal
Spasms
Flexor
Extensor
Mixed extensor/flexor
CLINICAL SEIZURES WITHOUT A CONSISTENT ELECTROCORTICAL SIGNATURE (*PATHOPHYSIOLOGY: PRESUMED NONEPILEPTIC*)
Myoclonic
Generalized
Focal
Fragmentary
Generalized tonic
Flexor
Extensor
Mixed extensor/flexor
Motor automatisms
Oral-buccal-lingual movements
Ocular signs
Progression movements
Complex purposeless movements
Electrical seizures without clinical seizure activity

Epileptic Syndromes

Few well-defined epileptic syndromes are found in the neonate (Berg et al., 2010); they range in severity from benign to those associated with poor outcomes. One of these syndromes is benign familial neonatal seizures. The seizures are characterized by focal clonic or focal tonic seizures that are electroclinical, have normal-background EEG activity, and typically have a good outcome (Plouin and Neubauer, 2012). There is a pattern of autosomal transmission based on a locus on chromosome 20 (Leppert et al., 1989; Quattlebaum et al., 1979). Singh and colleagues (1998) identified a submicroscopic deletion of chromosome 20q13.3 and encoded a novel voltage-gated potassium channel, KCNQ2, as the basis of this disorder. The disorder had been considered benign because initial reports suggested no long-term neurologic sequelae. However, subsequent studies indicated that not all affected infants have normal outcomes (Ronen et al., 1993).

Until recently, another benign syndrome, benign neonatal seizures, was recognized, but this designation has been eliminated as etiologies for these seizures have been identified (Berg et al., 2010). When considered as a syndromic group, these infants had also been characterized as having benign neonatal convulsions or benign idiopathic neonatal seizures (Plouin, 1992; Berg et al., 2010; Plouin and Anderson, 2002). As a group, the infants are typically full-term and products of normal pregnancy and delivery. The seizures are usually brief, most often clonic, and have their onset between 4 and 6 days of life. Dehan et al. (1977) described an interictal background EEG pattern that may present in these infants as *theta pointu alternant*, although it not considered specific to this disorder (Navelet et al., 1981; Plouin and Anderson, 2002) (see "Background EEG Activity" later).

There are two epileptic syndromes in the neonate associated with poor outcomes: early myoclonic encephalopathy (EME) (Aicardi, 1992; Aicardi and Goutieres, 1978) and early infantile epileptic encephalopathy (EIEE) (Ohtahara et al., 1978; Ohtahara et al., 1992). These are described and compared in Table 7.3 and have been reviewed by Aicardi and Ohtahara (2002). These disorders are characterized by suppression burst features on EEG and by early onset clinical seizures: erratic or fragmentary myoclonus in EME and tonic spasms in EIEE. There is a growing body of literature that has identified genetic mutations as the etiology of either syndrome recently summarized by Mizrahi and Milh (2012). Of note is the emerging evidence that a subset of neonates with encephalopathy, suppression burst

Table 7.3 Comparison of Early Myoclonic Encephalopathy (EME) and Early Infantile Epileptic Encephalopathy (EIEE)

	EME	EIEE
Age of onset	Neonatal period	Within first 3 months
Neurologic status	Abnormal at birth or at seizure onset	Always abnormal onset even prior to seizure onset
Characteristic seizure type	Erratic or fragmentary myoclonus	Tonic spasm
Additional seizure types	Massive myoclonus	Focal motor seizures
	Simple partial seizures	
	Hemiconvulsions	
	Infantile spasms (tonic)	Generalized seizures
Background EEG	Suppression-burst	Suppression-burst
Etiology	Inborn errors of metabolism	Cerebral dysgenesis
	Familial	Anoxia
	Cryptogenic	Cryptogenic
Natural course	Progressive impairment	Static impairment
Incidence of death	Very high, occurring in infancy	High, occurring in infancy, childhood, or adolescence
Status of survivors	Vegetative state	Severe mental retardation
		Quadriplegia and bed-ridden
Long-term seizure evolution	Infantile spasms	Infantile spasms
		Lennox–Gastuat Syndrome

Source: Based upon data from Aicardi (1992) and Ohtahara et al. (1992).

EEG, and electroclinical seizures of various types have a KCNQ2 mutation and potassium channelopathy (Numis et al., 2014; Serino et al., 2013; Weckhuysen et al., 2012, 2013).

Interictal EEG Features

Focal Sharp Waves

In older children and adults, a focal sharp wave or spike that may appear between the electrical seizures typically indicates the potential for an electrical seizure to arise from that region. However, in the neonate, interictal epileptiform discharges are rarely present to aid in diagnosis (Lombroso, 1985). Despite this caveat, isolated sharp waves may arise in the same region of eventual electrical seizure onset, and in these exceptional instances, they are considered epileptiform (**Figure 7.1**). However, sharp waves in the neonate typically are not considered evidence of a focal epileptogenic brain abnormality and therefore provide no useful information concerning the presence or absence of the potential for electrical or clinical seizures in a given infant. Focal sharp waves are discussed in detail in Chapters 5 and 6.

Background EEG Activity

The features of the background activity in infants suspected of having seizures may be helpful in diagnosis. The character of the background activity will provide information concerning the degree and distribution of brain injury and will provide the basis for consideration of possible diagnoses and prognosis (Bye et al., 1997; McBride et al., 2000; Ortibus et al., 1996). When recording infants suspected of having seizures, those with abnormal background EEG are more likely to eventually have electroclinical seizures than are those with a normal background (Glass et al., 2014; Laroia et al., 1998). In neonates with

documented clinical seizures, the degree of abnormality of the background activity may be associated with various seizures types: normal EEG background activity is more closely associated with electroclinical seizures, and abnormal background EEG activity is more closely associated with either clinical-only seizures (Mizrahi and Kellaway, 1987) or electrical-only seizures (Mizrahi and Kellaway, 1987; Pinto and Giliberti, 2001). The character of the background activity also may be helpful in the diagnosis of specific epileptic syndromes. The syndromes of EME and EIEE are associated with a suppression-burst pattern (Aicardi, 1992; Mizrahi and Milh, 2012; Ohtahara et al., 1992), as is the emerging syndrome of KCNQ2 neonatal encephalopathy (Numis et al., 2014; Serino et al., 2013; Weckhuysen et al., 2012, 2013), which eventually may be considered to be within the spectrum of one of the other suppression-burst syndromes. The background EEG activity of some of the infants with benign neonatal seizures has been described as a *theta pointu alternant* pattern (Dehan et al., 1977); although it is not considered specific for the disorder (Navelet et al., 1981; Plouin and Neubauer, 2012). This pattern is characterized by generalized theta activity that is occasionally associated with sharp waves. This activity is frequently asynchronous on the two sides and occurs discontinuously or in a pattern that alternates with periods of generalized voltage attenuation. That pattern can be present during wakefulness and all stages of sleep. *Theta pointu alternant* may be present for several days after seizures have resolved. While most often associated with the benign neonatal seizure syndromes, the pattern may also be present in infants with seizures of clearly defined etiology.

Ictal EEG Features

Electrical seizure activity consists of sustained rhythmic activity with various morphologies, amplitudes, and frequencies. Electrical seizures are often characterized in terms of their evolution of appearance. The minimal duration of a discharge to be considered an electrical seizure has been defined as 10 sec (Clancy and Legido, 1987), although this is admittedly arbitrary. Discharges of similar appearance but slightly shorter duration may have the same significance as those of 10 sec (Oliveira et al., 2000) (**Figure 7.2**) and have been referred to as brief ictal or interictal rhythmic discharges (BIRDs) (Shewmon, 1983) or brief electroencephalography rhythmic discharges (BERDs) (Nagarajan et al., 2011b).

While electrical seizure activity may be present in neonates before 34 to 35 weeks conceptional age (CA), it is less frequent in the premature infant than term (**Figure 7.3**). The precise CA at which the immature brain can consistently initiate and sustain electrical seizure activity has not been defined. With increasing age, however, electrical seizure activity becomes more frequent and may be of longer duration. Early reports suggested that when seizure activity does occur in preterm infants, the duration of electrical seizure activity is significantly shorter than full-term neonates (Scher et al., 1993) although more recent data suggest that the duration may not be significantly different when preterm and full-term infants are compared (Patrizi et al., 2003).

Patrizi and colleagues (2003) compared the features of electrographic seizures in preterm and full-term infants. For both groups, there was a relatively closer correlation between behavioral changes during the electrographic seizure when the background activity was normal or moderately abnormal than when background activity was severely abnormal. Preterm infants typically had regional onset to the seizure, whereas full-term infants most often had focal onset. For both groups the following features were similar: temporal region as the most frequent site of onset, seizure duration, and changing morphology of waveforms within the electrographic seizure. With both groups, there was no clear relationship between onset, morphology, frequency, or propagation patterns and etiology. Similarly, Okumura and colleagues (2008) noted that in preterm infants there was no clear relationship between clinical seizure manifestations and ictal EEG foci, duration of seizures, and morphology or propagation of ictal discharges.

All electrical seizure activity in the neonate begins focally, except for the generalized activity associated with some types of myoclonic jerks or with infantile spasms. The region of cortical involvement of the electrical seizure activity will determine the motor manifestations of the clinical seizures. The rate of repetition of the discharge will determine the rate of focal myoclonic and focal clonic activity: Slower discharges are associated with slow myoclonic movements (**Figure 7.4**); faster repetitive discharges are associated with sustained clonic activity (**Figure 7.5**); and at times, faster repetitive discharges are associated with focal tonic activity. Muscle groups involvement also will determine clinical manifestations. Smaller muscle groups, with smaller degrees of excursion, may be able to move more quickly in pace with rapid rhythmic EEG discharges than larger muscle groups.

Site of Onset

Electrical seizure activity in the neonate most often arises in the central (**Figure 7.5**) or temporal region (**Figure 7.6**) of one hemisphere or the midline central region (**Figure 7.7**). Less common sites of onset are occipital (**Figure 7.8**) and frontal regions (**Figure 7.9**).

Focality

Most often, in an individual infant, electrical seizure activity is unifocal—always arising from the same brain region. Seizures may also arise from more than one focal area so that, for example, the electrical seizures may arise from different foci at different times. They may also arise from two or

more foci at the same time, but with the two foci discharging asynchronously (**Figures 7.10–7.13**).

Frequency, Voltage, and Morphology

Frequency, voltage, and morphology may vary greatly within the same electrical seizure or from one seizure to the next in a given infant. The predominant frequency in a given seizure can be in the alpha, theta, beta, or delta ranges, or a mixture of these. The voltages of the activity may also vary, from extremely low (usually when faster frequencies are present) to very high (commonly seen when slow frequencies are present). The morphology of the electrical activity may also vary—consisting only of spikes of various durations, sharp waves, slow waves, or combinations of the waveforms within a given seizure. Examples of frequency, voltage, and morphology are shown in **Figures 7.14** to **7.19**.

Involvement of Specific Brain Regions

An individual electrical seizure, once begun, may be confined to a specific region (**Figure 7.20**) or it may spread to involve other regions (**Figure 7.21**). Spread may be by a gradual widening of the focal area; by abrupt change from a small regional focus to involvement of the entire hemisphere; by migration of the electrical seizure from one area of a hemisphere to another (either in a Jacksonian, but most often, in a non-Jacksonian fashion); or from one hemisphere to the other (**Figure 7.22**).

Evolution of the Electrographic Discharge

Some electrical seizure activity may begin abruptly with frequencies, voltage, and morphology, which remain fairly constant throughout the seizure. However, more often, seizures undergo an evolution in appearance with their character changing throughout their course (**Figures 7.23** and **7.24**). The changing character throughout an electrical seizure helps in differentiating electrical seizure activity from other nonepileptic rhythmic activity or artifact.

Special Ictal Patterns

There are some unique ictal patterns that occur in neonates with severe encephalopathies: electrical "seizures of the depressed brain" and "alpha seizures discharges." Electrical seizures of the depressed brain are seen in neonates whose background EEG activity is depressed and undifferentiated (**Figure 7.25**). The discharges are typically low in voltage, long in duration, highly localized, may be unifocal or multifocal, and show little tendency to spread or otherwise change (Kellaway and Hrachovy, 1982). This seizure pattern typically is not accompanied by clinical seizure activity and its presence suggests a poor prognosis.

The sudden but transient appearance of rhythmic activity in the alpha frequency has, in the past, been referred to as alpha seizure activity (Knauss and Carlson, 1978; Watanabe et al., 1982; Willis and Gould, 1980) (**Figures 7.26** and **7.27**). This pattern is characterized by the sudden appearance of rhythmic 8 to 12 Hz, 20 to 70 μV activity typically in one temporal or central region; however, it can also evolve from activity that is more clearly epileptiform. In addition, it may occur simultaneously, but asynchronously, with other electrical seizure activity (**Figure 7.28**). Its presence is indicative of severe encephalopathy and suggests a poor prognosis. This pattern may also be present in the absence of any clinical seizures. This paroxysmal alpha pattern should be differentiated from virtually continuous rhythmic, low-voltage alpha activity, which is a rare finding in the neonate associated with congenital heart disease, chromosomal abnormalities, and administration of some CNS-active medications (Hrachovy and O'Donnell, 1996).

Generalized Electrical Seizure Patterns

Electrographic events that are considered generalized seizure patterns are rare in the neonate and are associated with only a few specific clinical seizure types. Generalized sharp transients may be associated with generalized myoclonus (**Figure 7.29**). Spasms may occur in association with generalized voltage attenuation (**Figure 7.30**).

Electrical Seizure Activity and Medication Effects

An important effect medication may have on electroclinical seizures is the elimination of clinical seizures while electrical seizures persist. In addition to the occurrence of both electrical seizure activity of the depressed brain and the alpha seizure pattern discussed earlier, electrical seizure activity without clinical seizures may be present in infants treated with AEDs. A common situation occurs during the acute administration of AEDs in an infant with electroclinical seizures. This may result first in control of the clinical seizures with persistence of the electrical seizure (**Figure 7.31**). The phenomenon has been termed "decoupling" of the clinical from the electrical seizure (Mizrahi and Kellaway, 1987) described by others as "electroclinical disassociation" (Weiner et al., 1991) and "uncoupling" (Scher et al., 2003). After continued AED administration, the electrical seizure activity may become modulated and may eventually be eliminated. However, frequently increasing AED dosage or additional agents may not completely eliminate electrical seizure discharges. In instances in which electrical seizures are controlled, they may recur without clinical accompaniment.

Another circumstance in which electrical seizures occur without clinical seizures because of pharmacologic therapy is when infants are paralyzed for respiratory ventilation and other medical reasons. Obviously, an infant who is paralyzed cannot manifest motor signs of seizures. This is of clinical concern since neonates who require ventilation may also be at risk for encephalopathy associated with seizures.

Electrical Seizure Activity and Hypothermia

Therapeutic hypothermia for infants with encephalopathy of hypoxic-ischemic origin has become relatively routine in high acuity nurseries, and electroclinical, and more often, electrical-only seizures, may occur in these infants (Glass et al., 2014; Low et al., 2012; Shah et al., 2014; Wusthoff et al., 2011). Many clinical protocols include some form of neurophysiological monitoring-either amplitude integrated EEG (aEEG) or continuous EEG (cEEG). At onset of hypothermia, some infants may experience seizures as part of their encephalopathy and are typically treated with AEDs concurrently with hypothermia. It is unclear whether hypothermia has a direct impact on electrical seizure activity, although it does affect metabolism and subsequent availability of administered AEDs. Overall, the seizure burden for infants undergoing hypothermia appears less compared to those without this therapy but with similar degree of brain injury, perhaps due to shorter seizure duration (Low et al., 2012). The risk for seizure onset may be early in the cooling process or during rewarming with events characterized as "rebound seizures" (Kendall et al., 2012). The occurrence of seizures during hypothermia is still unpredictable and neurophysiologic monitoring is typically conducted from the cooling through the rewarming period (Boylan et al., 2015) (**Figure 7.32**).

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Figure 7.31 Response to acute antiepileptic drug therapy.

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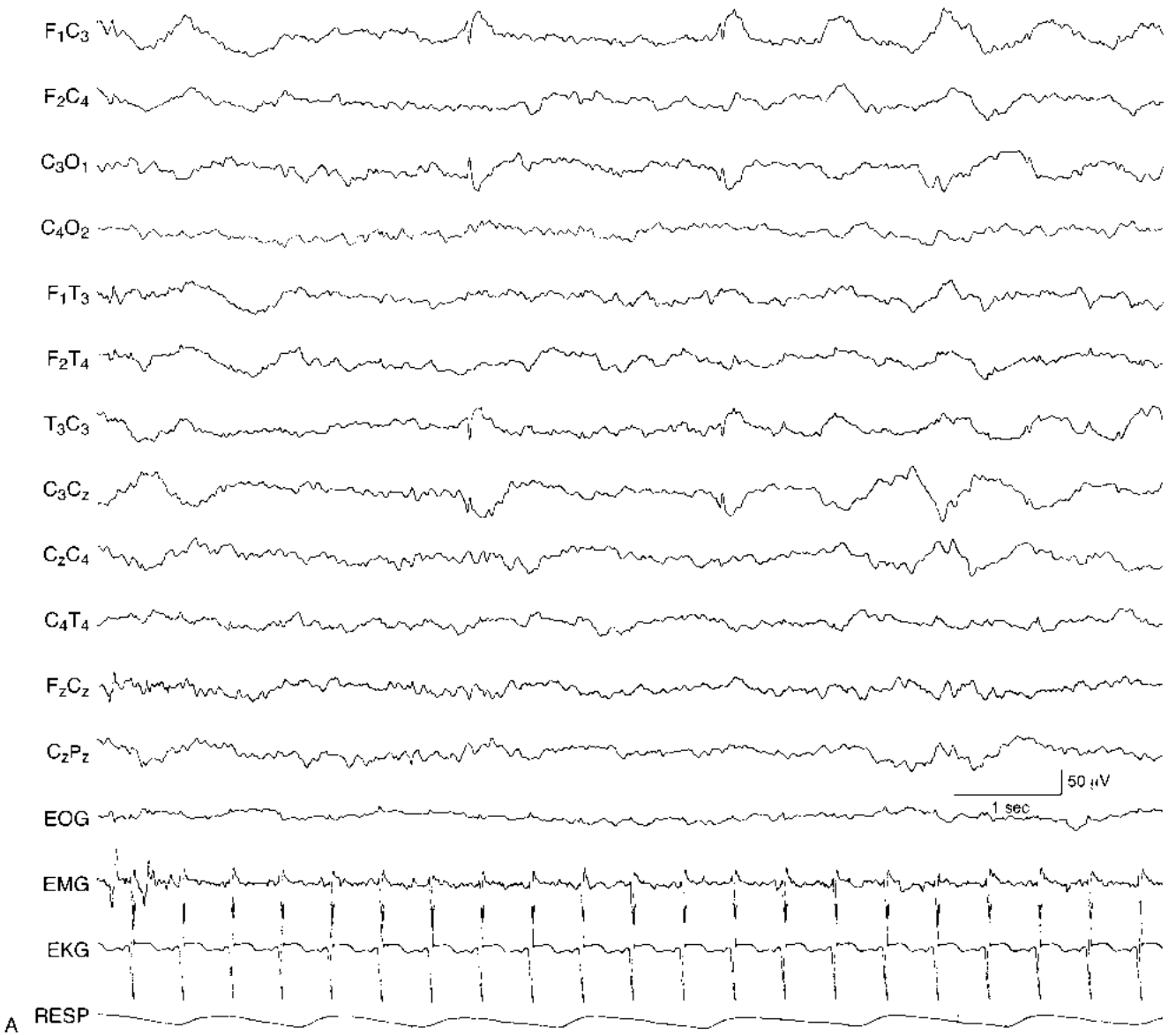
Figure 7.32 Electrical seizure emerging during hypothermia protocol.



A

Figure 7.1 (A) and (B) Relationship of interictal spikes to seizure activity. (A) There are intermittent low-voltage spikes in the left central region; their occurrence waxed and waned in other portions of the recording (not shown). (*continued*)

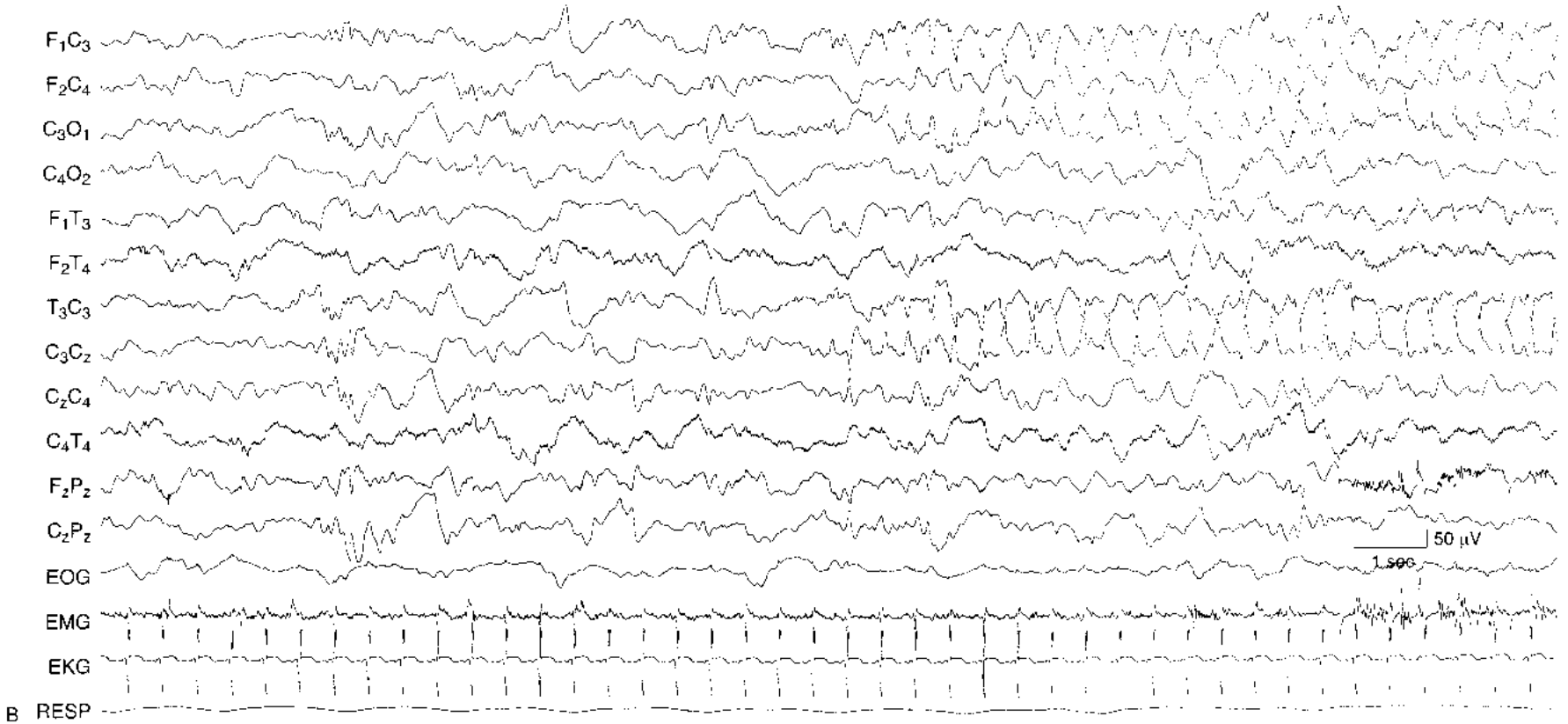


Figure 7.1 (*continued*) **(B)** Later in the recording an electrical seizure arises from the same region associated with focal clonic activity of the right arm. The background EEG activity is within the range of normal variation (not shown). This EEG is from a 41-week CA infant with a left frontal parietal lobe infarction.

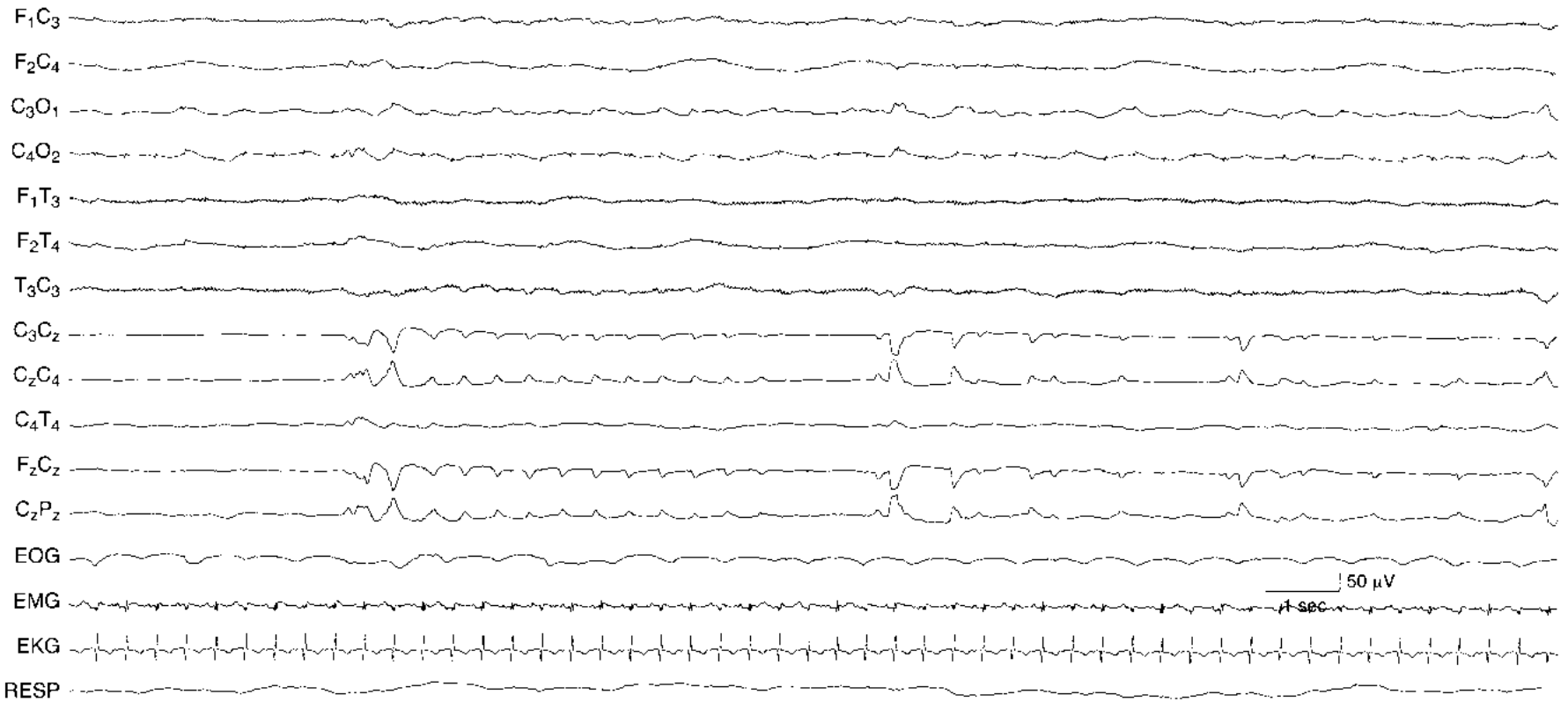


Figure 7.2 Discharge duration defines the seizure. A brief discharge is present in the midline central region with a duration of less than 10 sec. There are some less regularly occurring sharp waves after the discharge. The background activity is depressed and undifferentiated in this 40-week CA infant with hypoxic-ischemic encephalopathy.

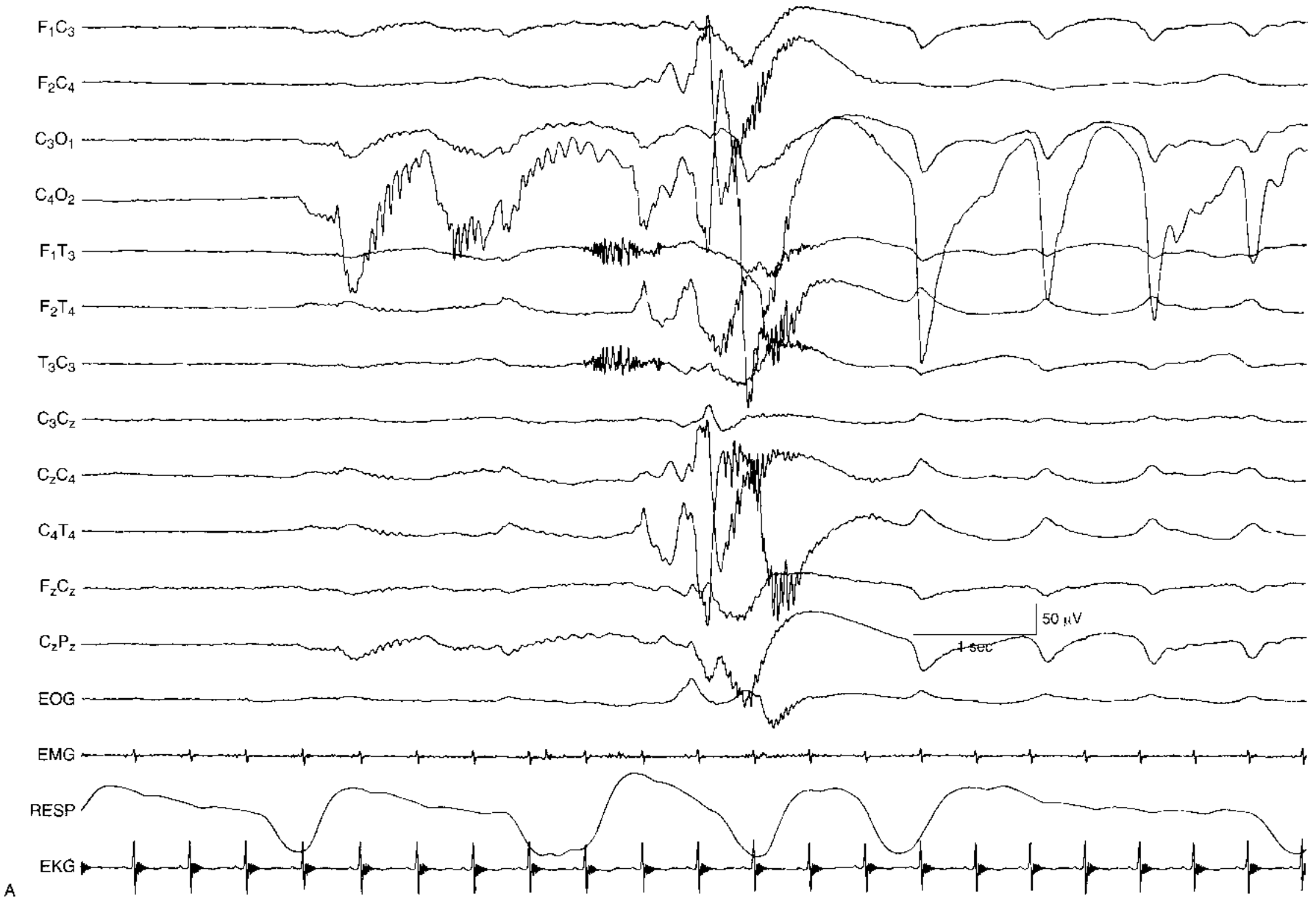
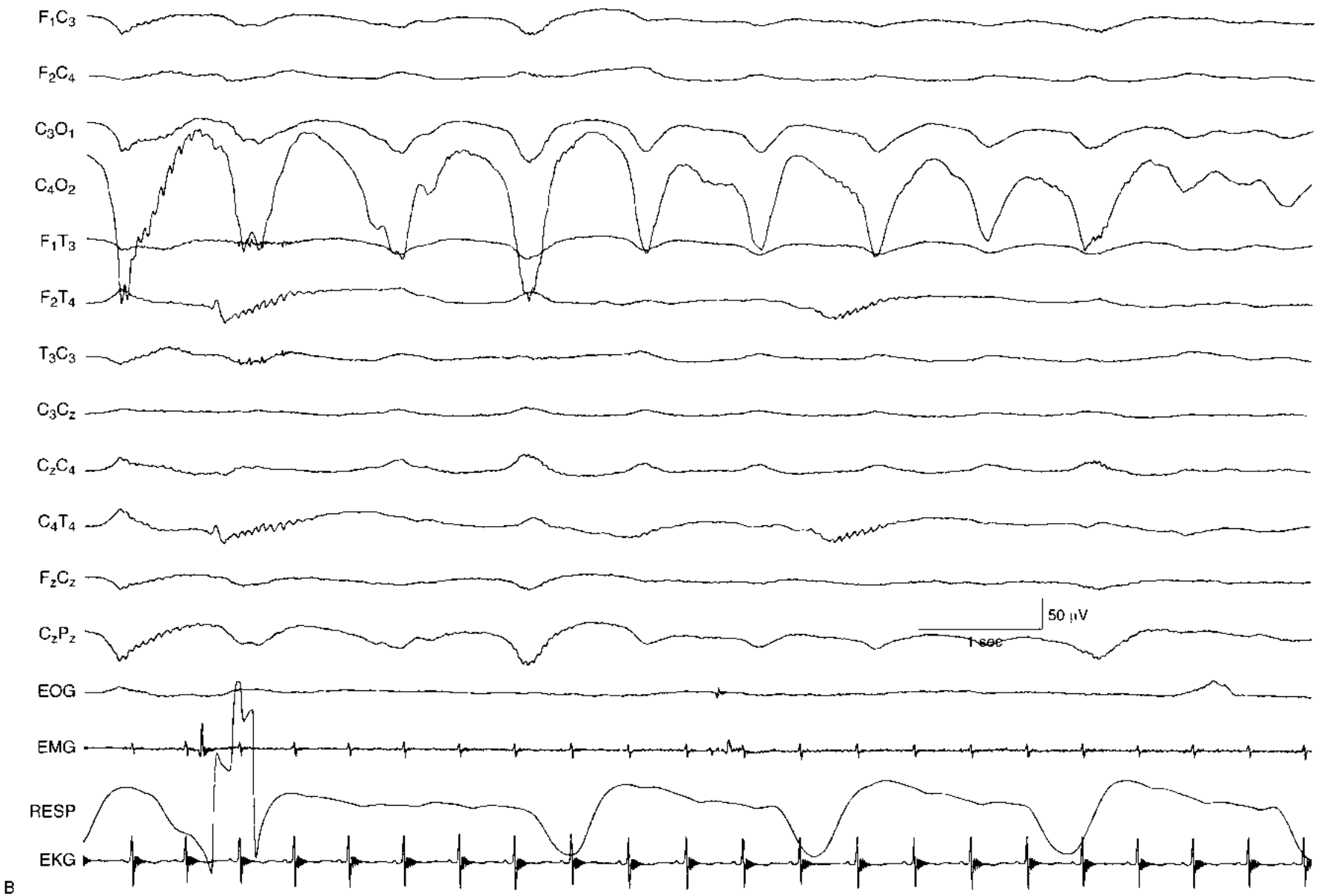


Figure 7.3 (A)–(E) Seizure discharges in the premature infant. (A) An electrical seizure begins in the right occipital region in this 28-week CA infant. The segments **(A)** to **(C)** show continuous recordings. (*continued*)



B

Figure 7.3 (*continued*) **(B)** The discharge persists with gradually reducing amplitude, although the amplitudes remain high. (*continued*)

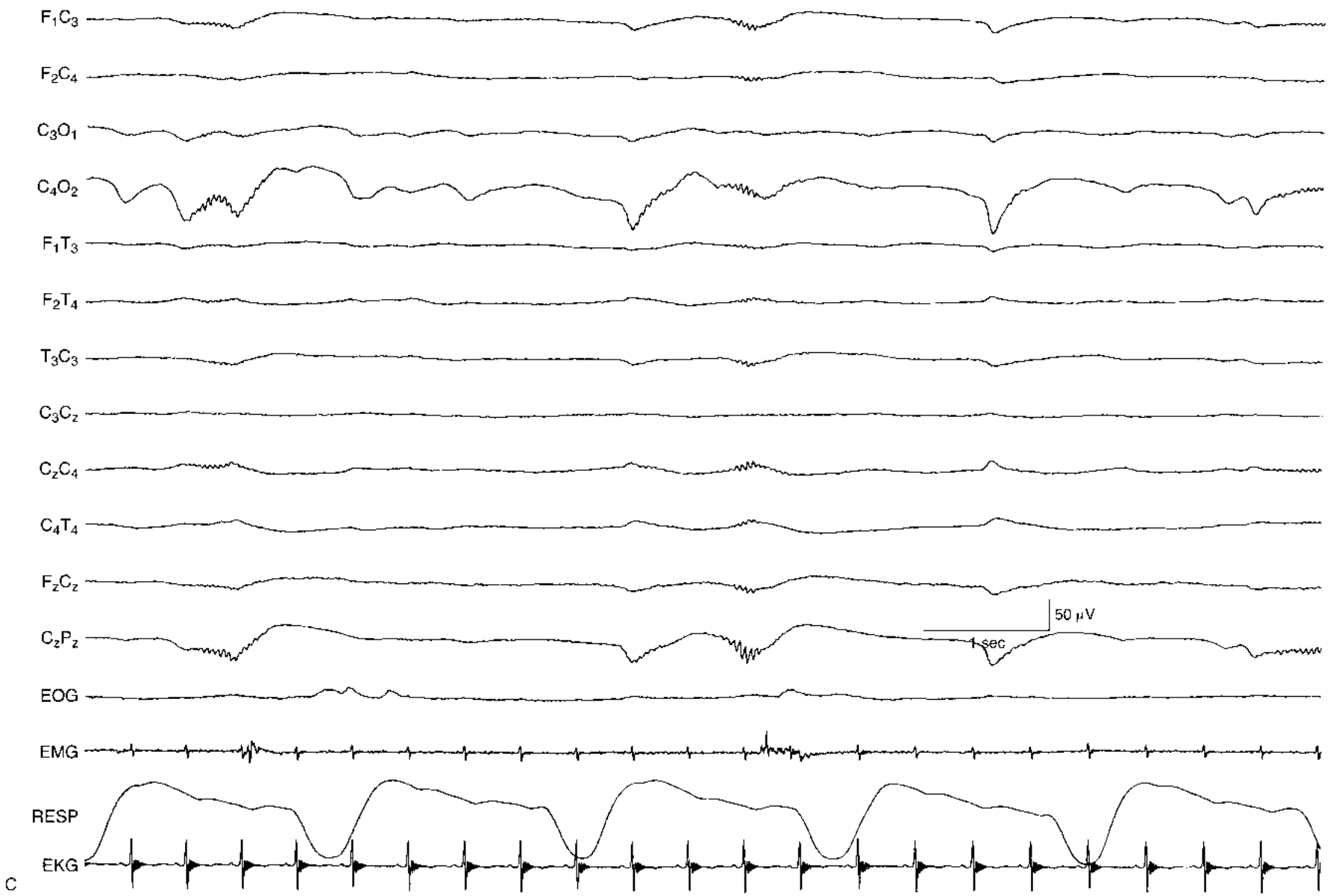


Figure 7.3 (*continued*) **(C)** The seizure discharge subsides. (*continued*)

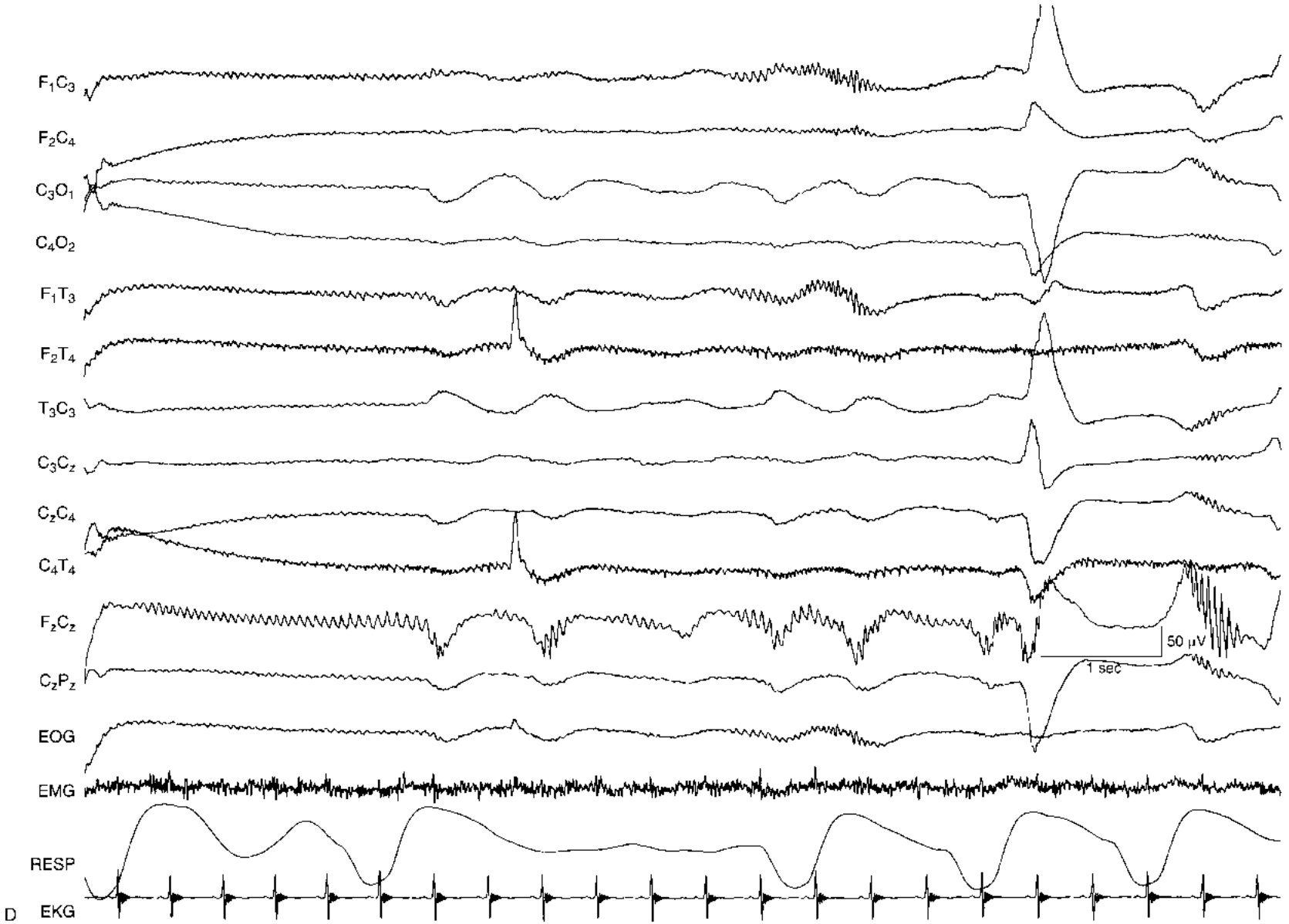


Figure 7.3 (*continued*) **(D)** During the same recording, there is rhythmic alpha activity in the midline frontal region lateralized to the left. (*continued*)

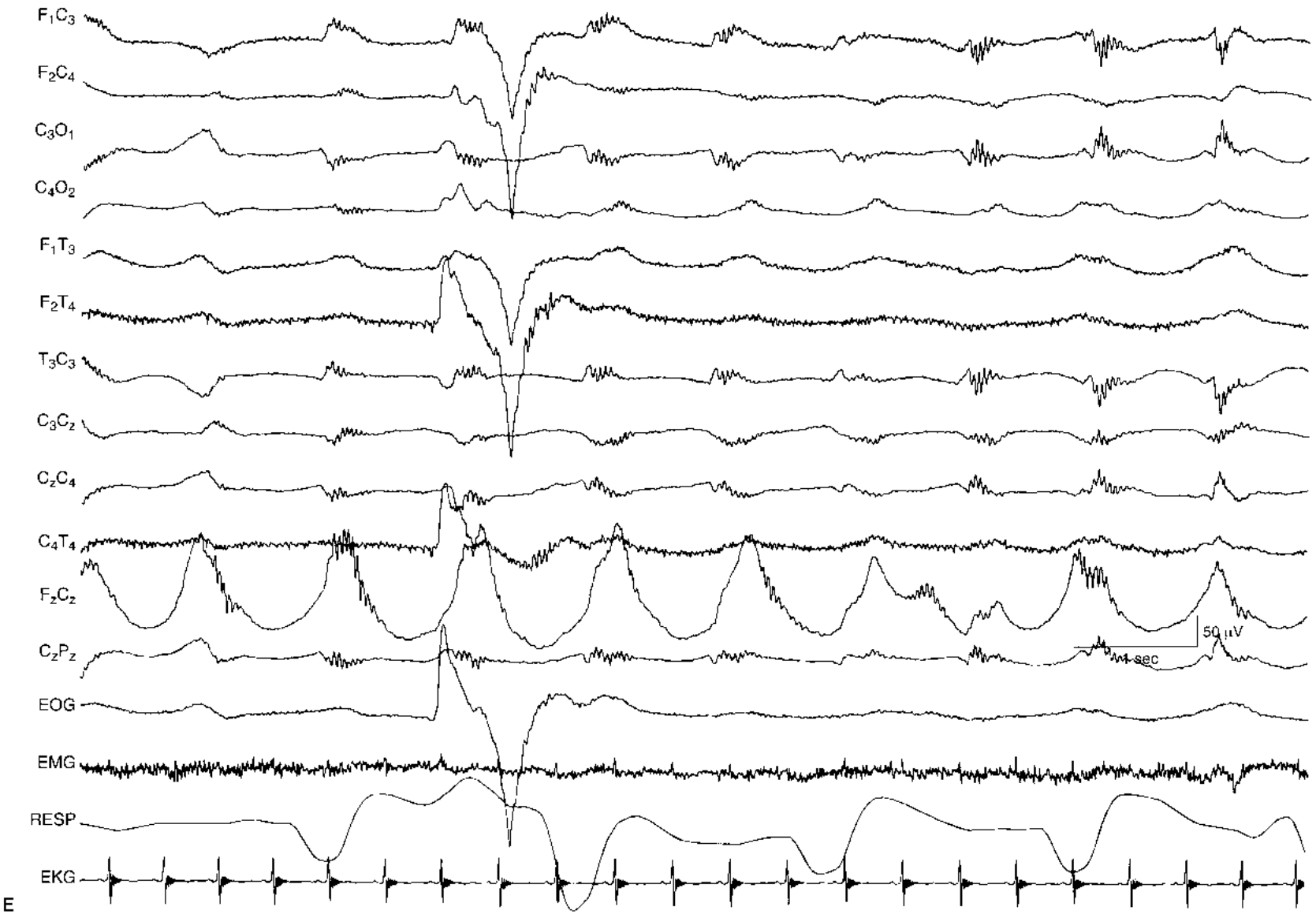


Figure 7.3 (*continued*) **(E)** This segment is continuous with **(D)** showing the evolution of the seizure activity to recurrent rhythmic bursts superimposed upon high voltage slow sharp waves. No clinical events occurred with any of the electrical seizure activity.

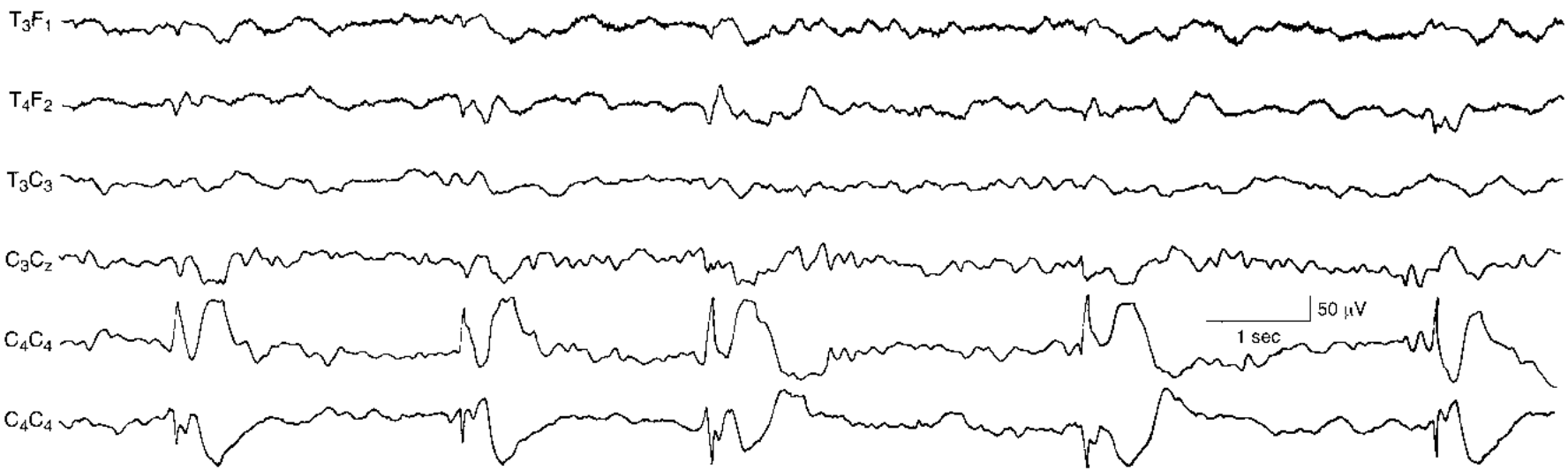


Figure 7.4 Seizure discharges with focal myoclonus. Spike and slow-wave discharges recur at a slow but regular rate in the right central region. A single, slow, myoclonic flexion of the left arm occurred in close association with each spike and slow-wave discharge. The background activity is within the range of normal variation in this term infant. This is a selected sample from a 12-channel EEG recording.

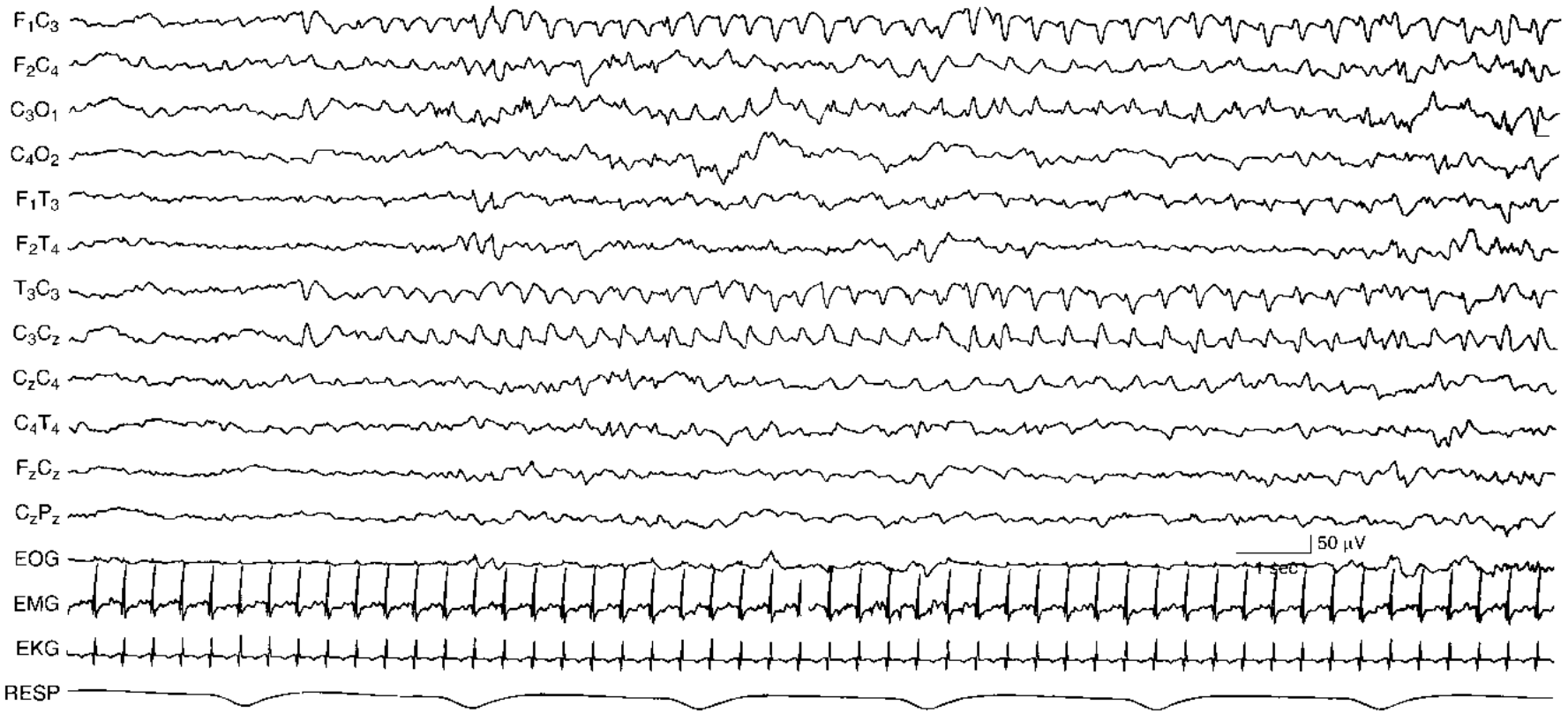


Figure 7.5 Central onset of electrical seizure activity. Rhythmic sharp waves arise in the left central region and remain confined to that region. This electrical activity occurred with a clinical seizure characterized by clonic activity of the right hand in this 40-week CA infant with a left frontal lobe infarction. When the electrical seizure discharge was correlated with computed tomography (CT) findings, the site of ictal onset coincided with the periphery of the lesion—a region that perhaps was more capable of generating such a discharge than the most devitalized cortex at the center of the infarct. The EEG background activity is within the range of normal variation (not shown).

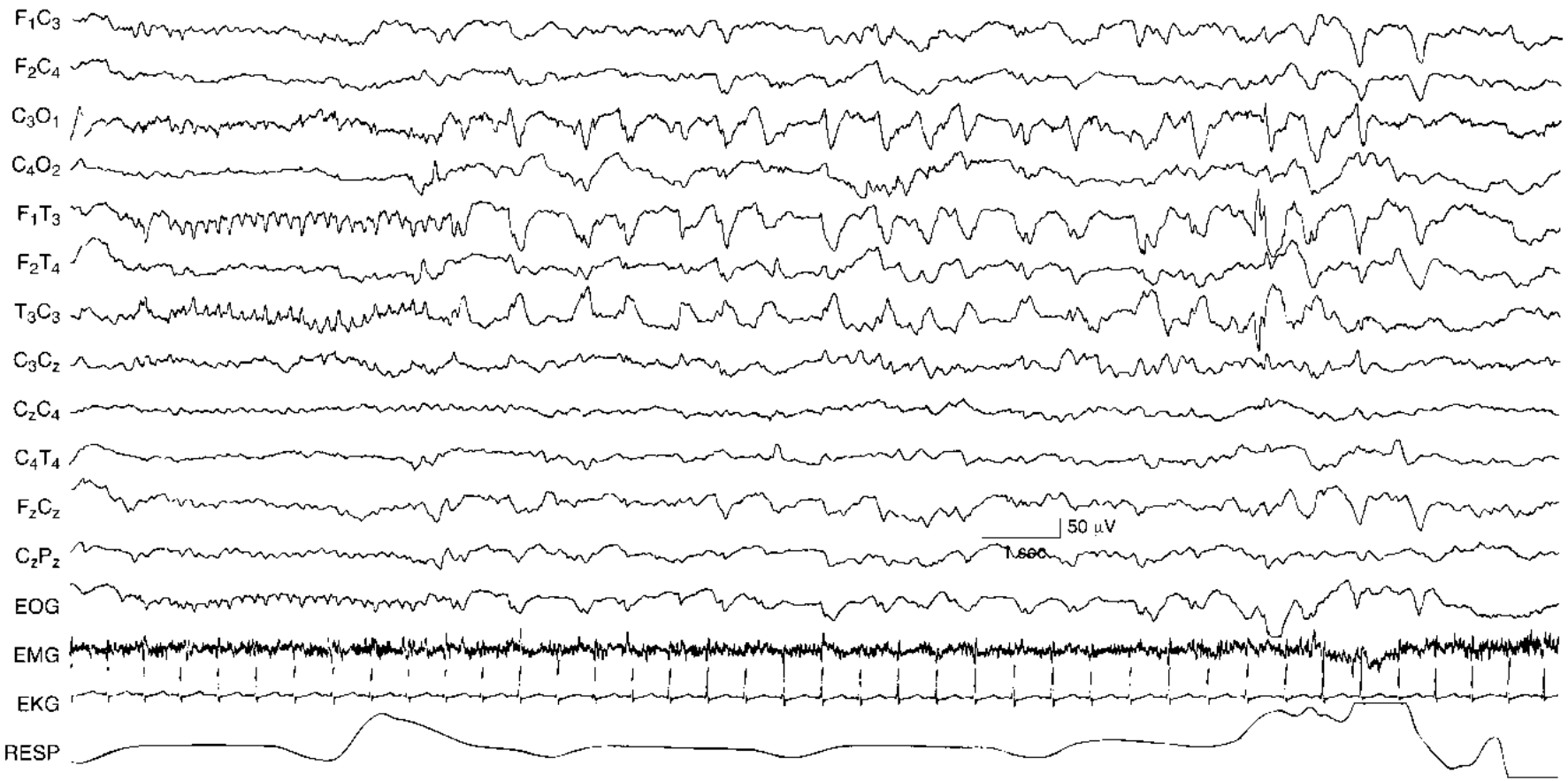


Figure 7.6 Temporal onset of electrical seizure activity. The electrical seizure begins in the left temporal region as low voltage, fast, rhythmic sharp-wave activity, and then abruptly changes to rhythmic, moderately high voltage slow activity with sharply contoured waves involving more of the posterior regions on that side. The seizure is brief and in the final few seconds of the segment, there is little post-ictal change. No clinical seizures occurred during this brief electrical event. The interictal EEG background activity is within the range of normal variation (not shown). This sample is from a 40-week CA infant with an intracerebral hemorrhage in the left posterior temporal lobe.

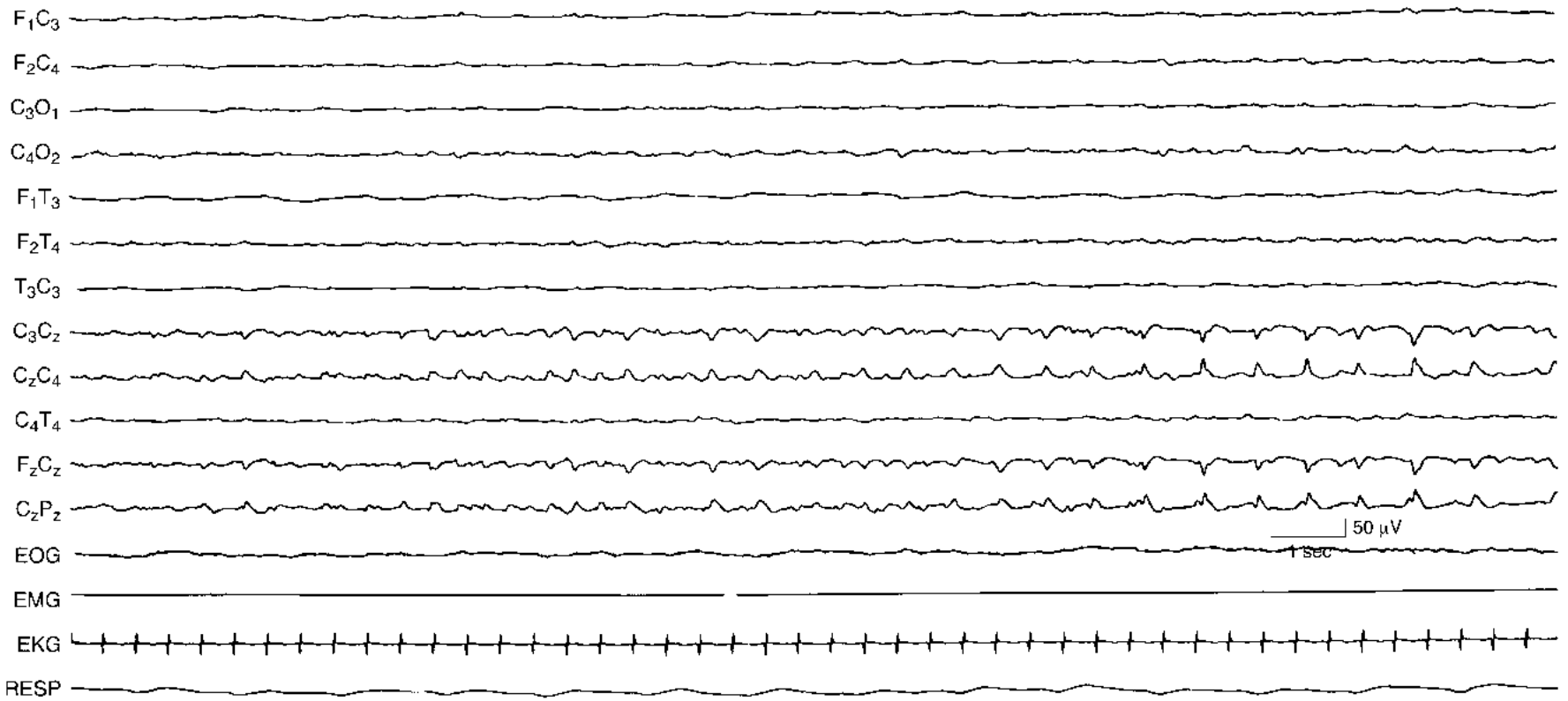


Figure 7.7 Midline central onset of electrical seizure activity. Low voltage, rhythmic sharp wave activity arises in the midline central region and remains confined to that region throughout the seizure. There is little evidence of this activity from electrodes covering adjacent brain regions. The background EEG activity is depressed and undifferentiated. The electrical event can be described as a "seizure discharge of the depressed brain." No clinical seizures occurred in association with the electrical seizure activity. This EEG is from a 38-week CA infant with diffuse cerebral ischemia.

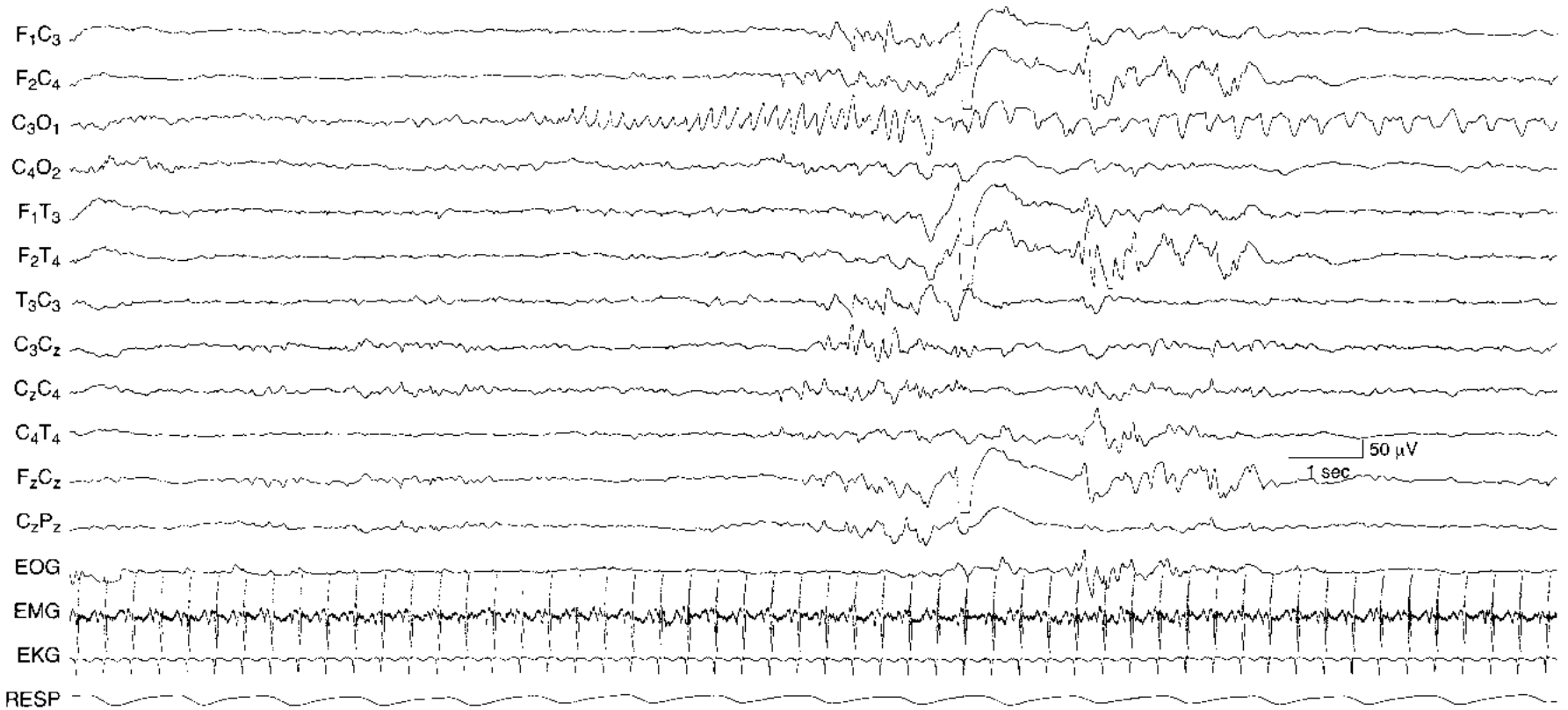


Figure 7.8 Occipital onset of electrical seizure activity. Rhythmic sharp waves arise from the left occipital region with evolution to slower rhythmic wave forms not associated with clinical seizures. The interictal background activity is characterized as a suppression-burst pattern. This EEG is from a 40-week CA infant supported by ECMO with meconium aspiration, right hemispheric intracerebral hemorrhage, subarachnoid hemorrhage, and congenital syphilis.

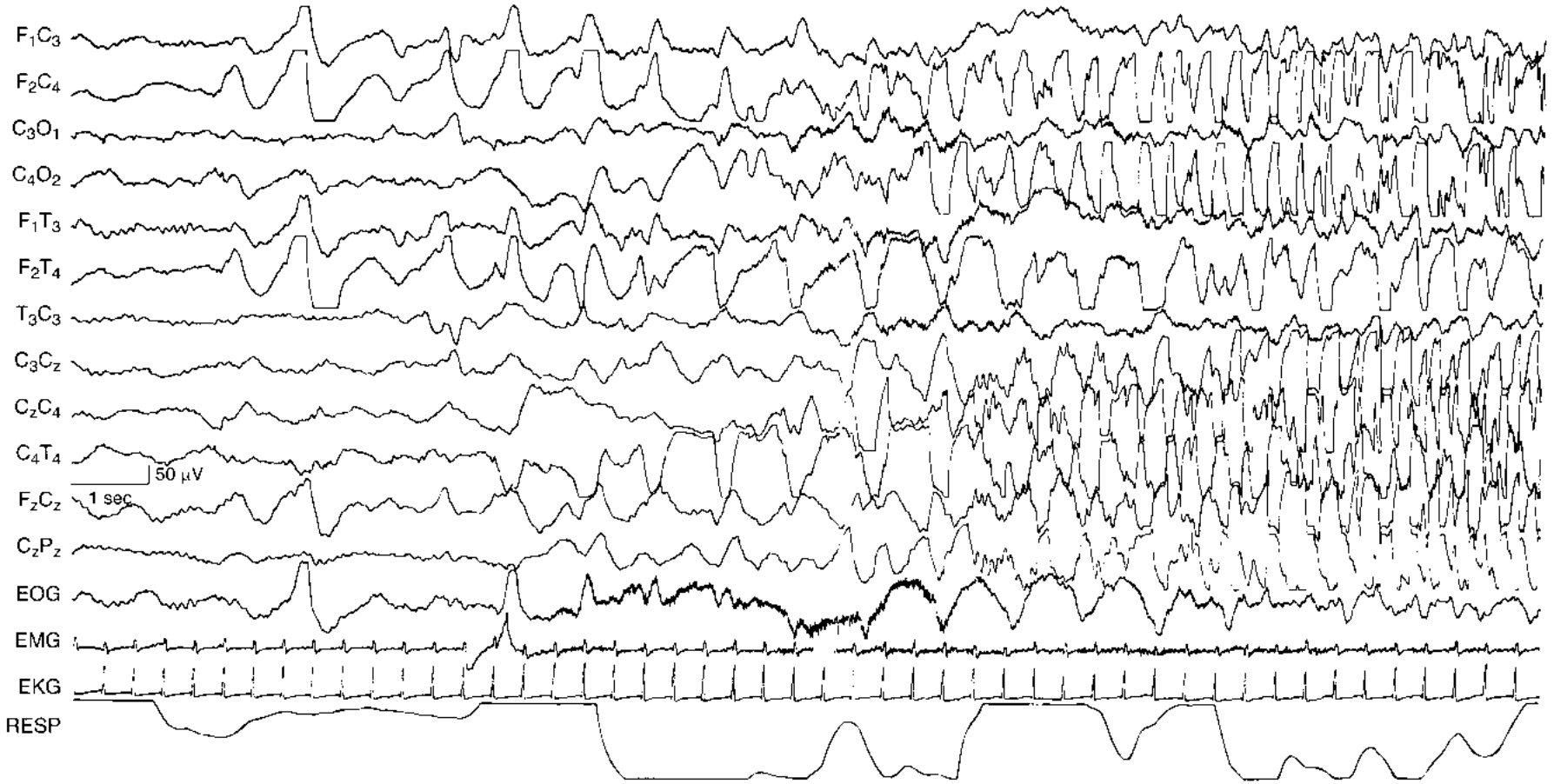


Figure 7.9 Frontal onset of electrical seizure activity. High voltage, repetitive, slow sharp waves arise in the right frontal region and, after several seconds, appear as faster and sharper discharges that have spread to the right central region. With electrical seizure onset, a clinical seizure begins, characterized by initial extension of the left arm and leg, followed by clonic jerking of the left hand and foot. The interictal EEG background activity is within the range of normal variation (not shown). This occurred in a 40-week CA infant with trisomy 9 and multiple congenital anomalies including tetralogy of Fallot, absent right kidney, and dysmorphic facial features.

Figure 7.10 Multifocal electrical seizure activity. Seizure discharges occur simultaneously, but asynchronously in the central regions on the two sides. No clinical seizures occurred in association with these electrical discharges—the infant had been treated with phenobarbital prior to EEG recording. The interictal EEG background activity is depressed and unidifferentiated (not shown). This EEG is recorded from a 39-week CA infant with hypoglycemia.

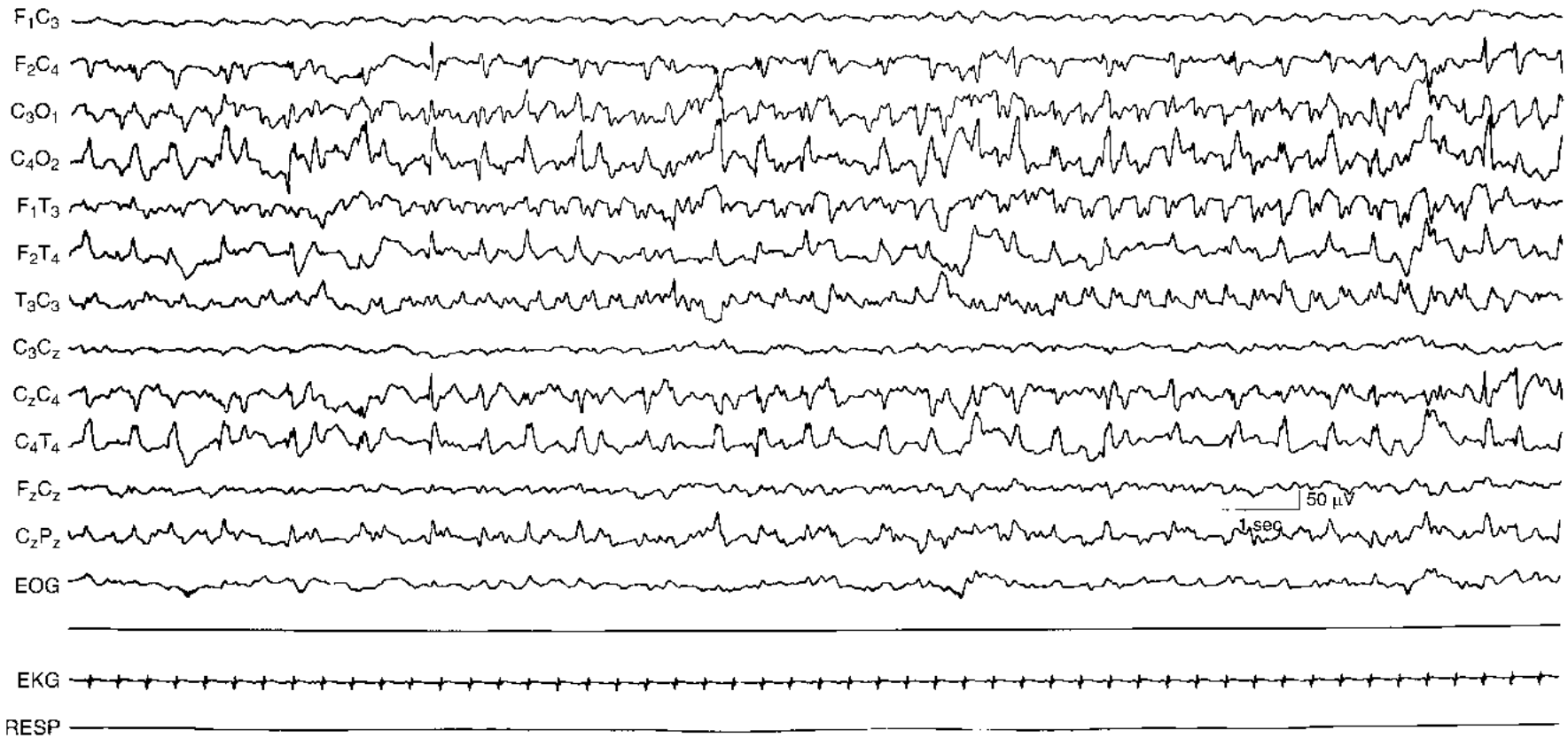


Figure 7.11 Multifocal electrical seizure activity. Initially, rhythmic, moderate voltage, sharp wave activity arises from the right central-temporal region and is sustained, relatively unchanged. Another, seizure discharge arises independently from the left temporal region, characterized by low voltage, sharp wave, and slow wave activity with complex morphology. No clinical seizures occurred with these electrical seizures. The EEG background activity is depressed and undifferentiated (not shown). This EEG is from a 39-week CA infant with meconium aspiration, cardiac failure and persistent cyanosis, and hypoxemia requiring ECMO.

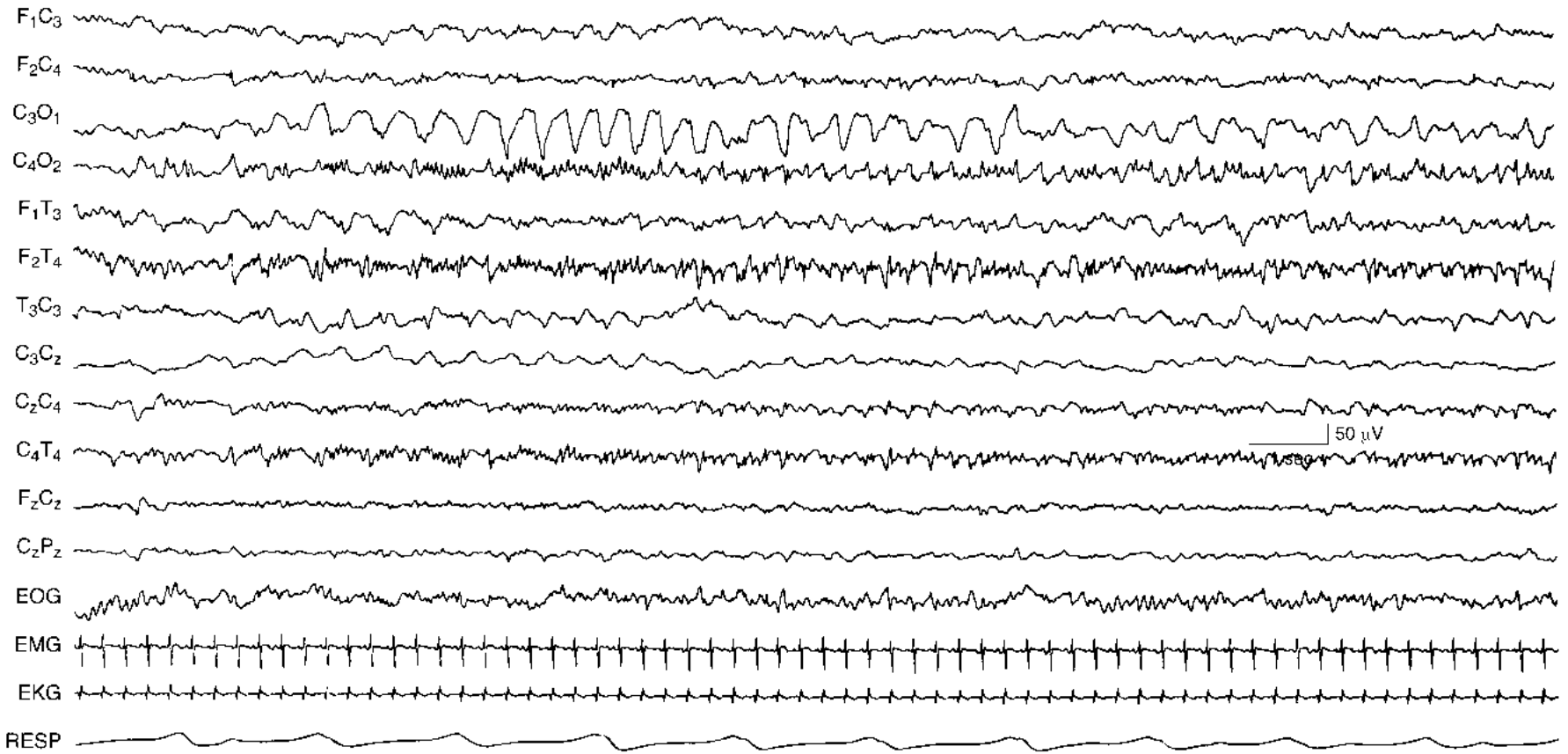


Figure 7.12 Multifocal electrical seizure activity. Two seizure foci are present, each with distinct morphology. There is rhythmic, slow, moderate voltage activity in the left occipital region, and there is independent, low to moderate voltage, rhythmic, fast activity in the right temporal occipital region. The background activity is depressed and undifferentiated (not shown). No clinical seizures occurred with the electrical seizures. This EEG is from a 4-week-old infant, born at 38 weeks gestational age (42 weeks CA) with pneumococcal meningitis. Neuroimaging revealed bilateral subdural fluid collections, greater on the right; bilateral parasylvian petechial hemorrhages and bilateral cerebral edema.

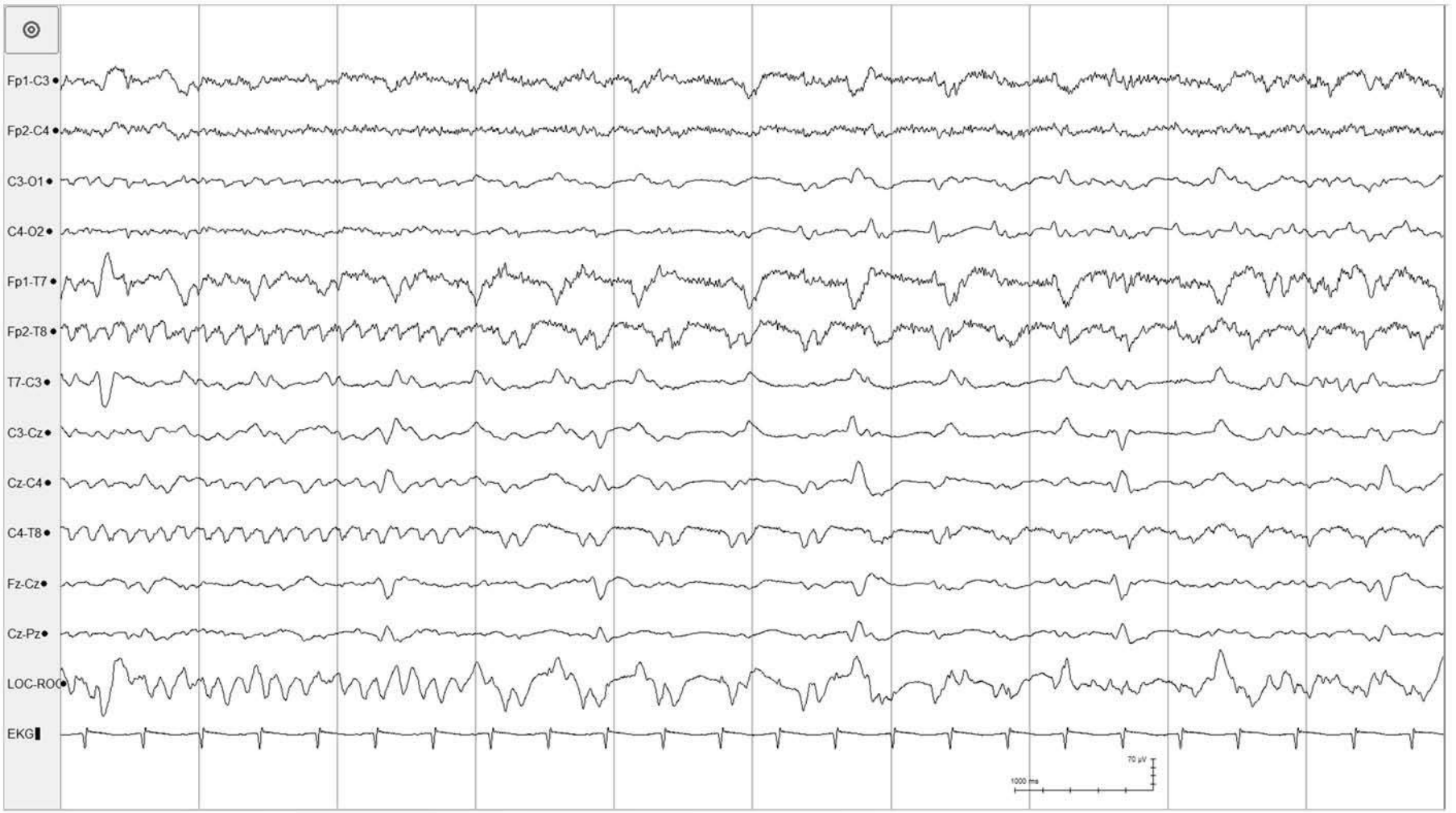


Figure 7.13 Multifocal electrical seizure activity. Electrical seizure activity is present independently in the right temporal and left frontal-temporal regions. The discharge on the right changes in morphology and frequency while the discharge on the left is more constant. This occurred in a 39-week CA infant with hypoxic ischemic encephalopathy and a background that is depressed and undifferentiated.

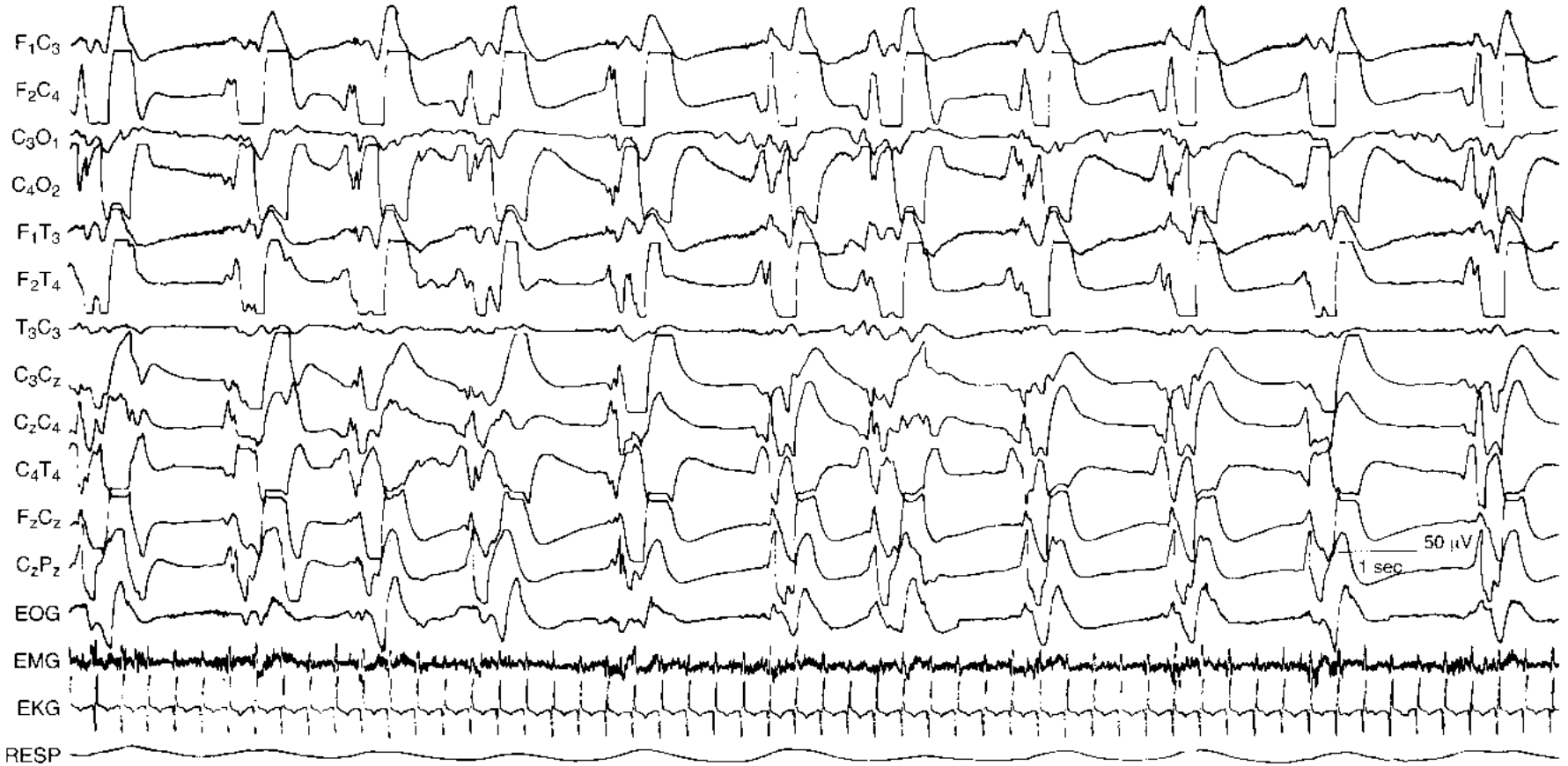


Figure 7.14 High-voltage seizure activity. High voltage, repetitive, sharp and slow waves, mixed with some spike and slow waves, are present in the right central region with involvement of almost all of the hemisphere on that side. A clinical seizure coincided with the electrical seizure discharge and was characterized by focal clonic activity of left leg, face, and hand. The background EEG activity was depressed and undifferentiated (not shown). This EEG is from a 40-week CA infant with subarachnoid hemorrhage.

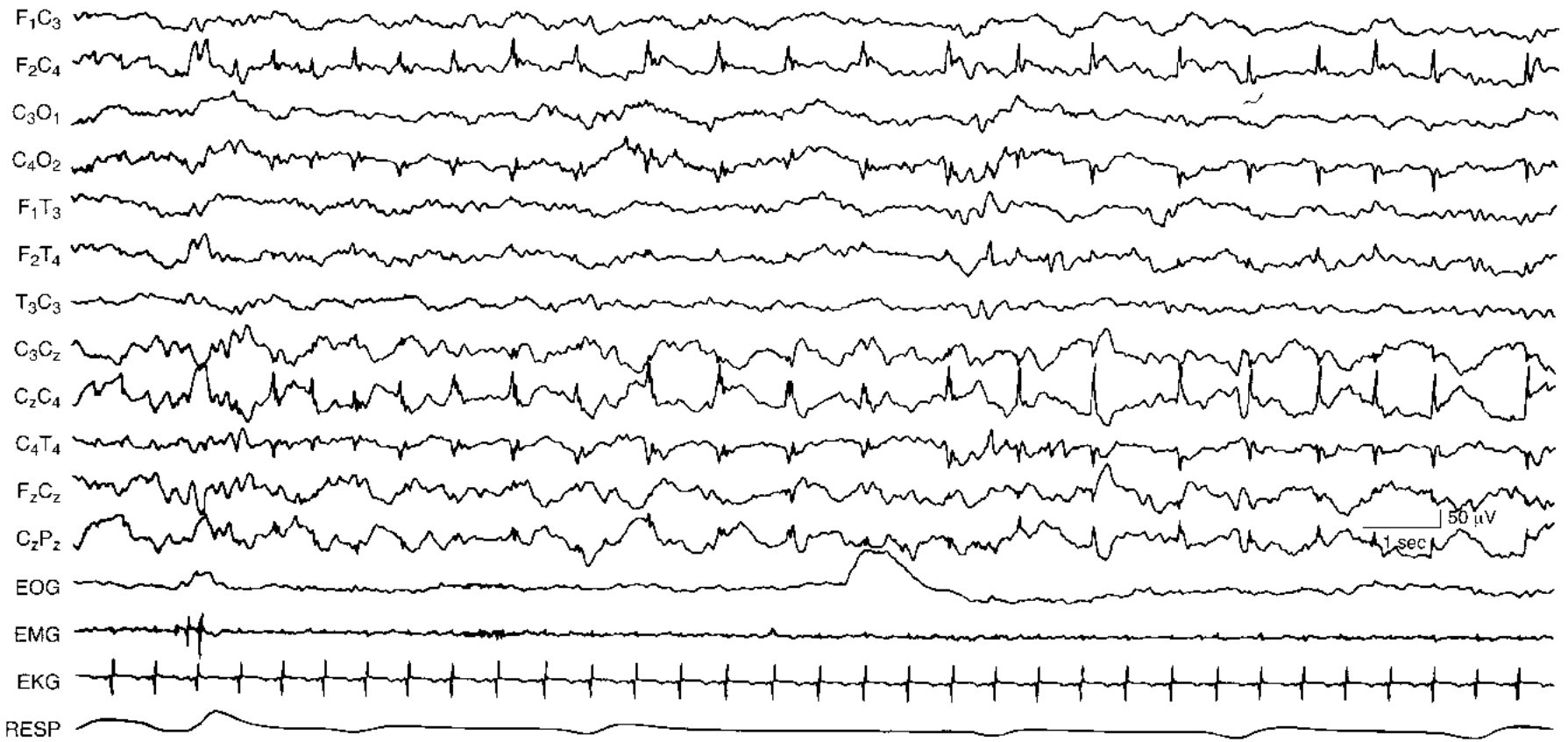


Figure 7.15 Spike morphology of seizure discharges. A seizure discharge arises from the right central region consisting of repetitive spike discharges occurring in association with a clinical seizure characterized by focal clonic activity of the left foot. The EEG background activity is undifferentiated (not shown). This EEG is from a 41-week CA infant with group B streptococcal meningitis and associated cerebral infarction of the right posterior temporal and occipital lobes.

Figure 7.16 Spike morphology of seizure discharges. Repetitive spike and slow waves arise in the right central-temporal region in association with a clinical seizure characterized by left arm, leg, and face focal clonic activity. The interictal background activity was within the range of normal variation for age (not shown). This EEG is from an 8-week old, 34-week gestational age (42-week CA) infant with non-accidental head trauma resulting in an intracerebral hemorrhage in the right frontal lobe.

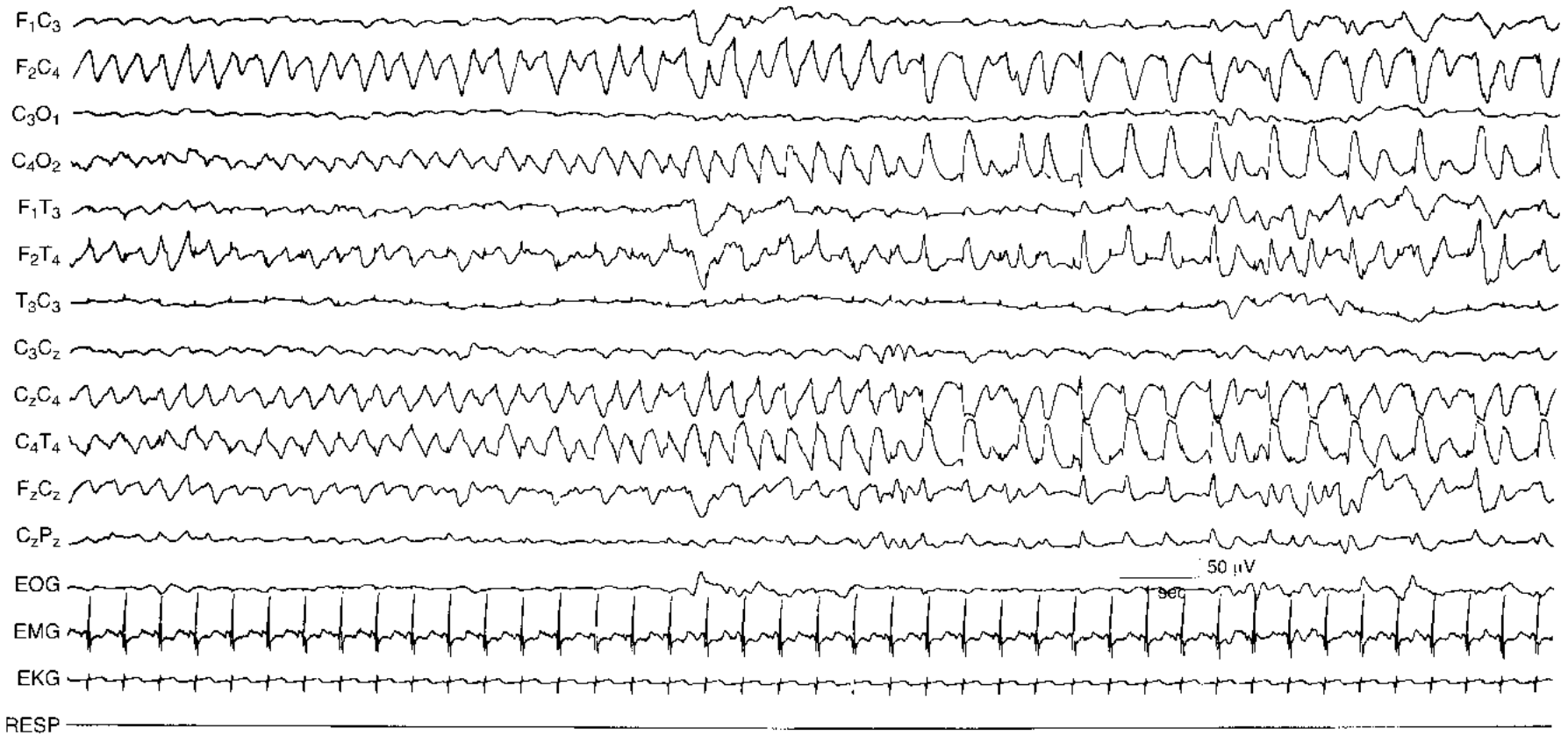


Figure 7.17 Slow wave morphology of seizure discharges. Rhythmic, moderate voltage, 3 Hz activity is present in the right central region and evolves to seizure activity which is higher in voltage, slower and mixed with spike discharges. This occurred in association with focal clonic activity of the left hand. The background EEG activity is depressed and undifferentiated (not shown). This EEG is from a 38-week CA with meconinum aspiration, persistent hypoxemia, and ECMO support.

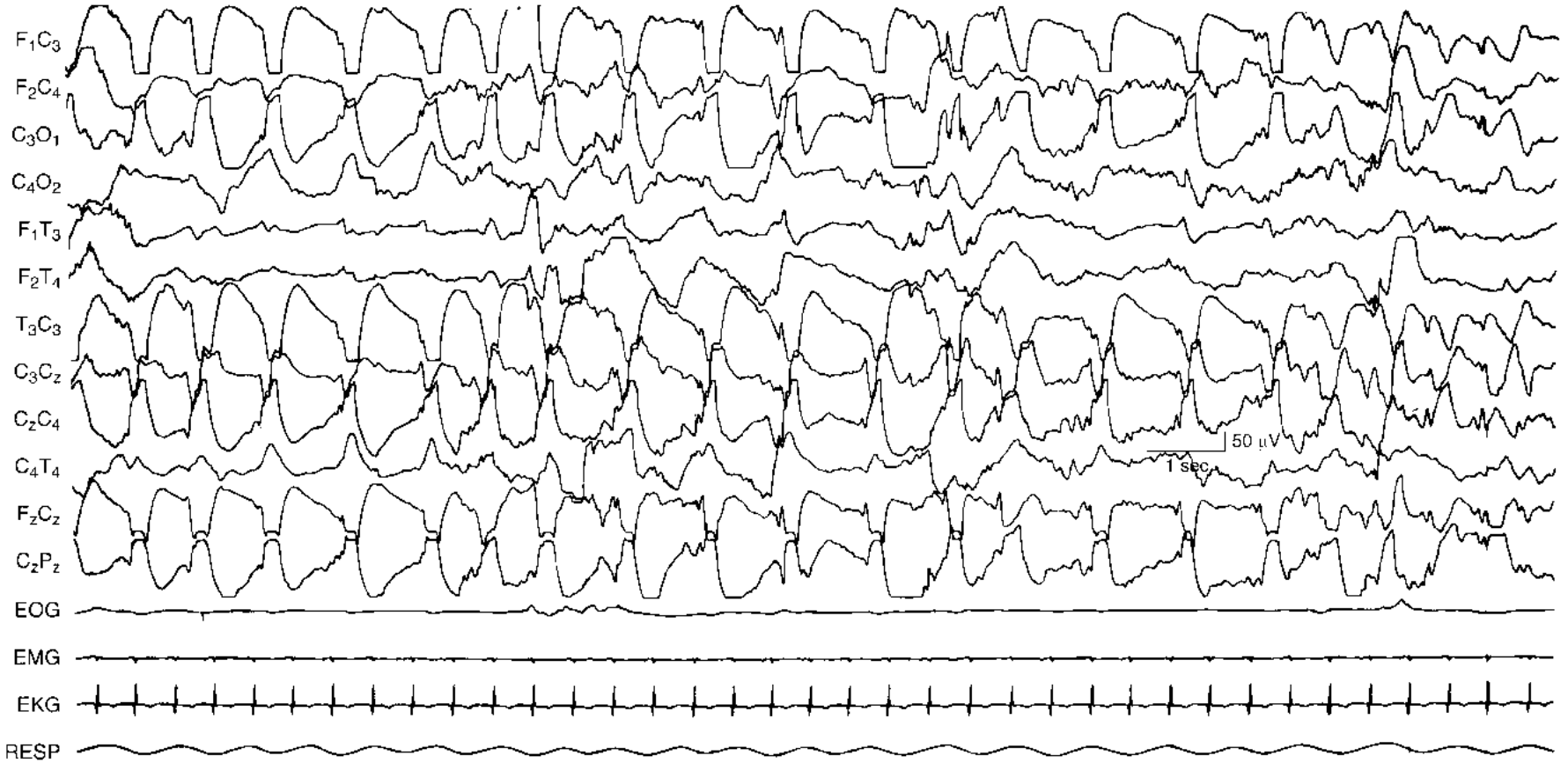


Figure 7.18 Slow wave morphology of seizure discharges. High voltage, very slow rhythmic activity, mixed with occasional spikes, is present in the left central region that occurred in association with the focal clonic activity of the face, arm, and leg on the right. The interictal EEG background activity is within the range of normal variation (not shown). This EEG is from a 42-week CA with intraventricular hemorrhage in the left lateral ventricle near the head of the caudate and cerebral edema in the left frontal lobe adjacent to the hemorrhage.

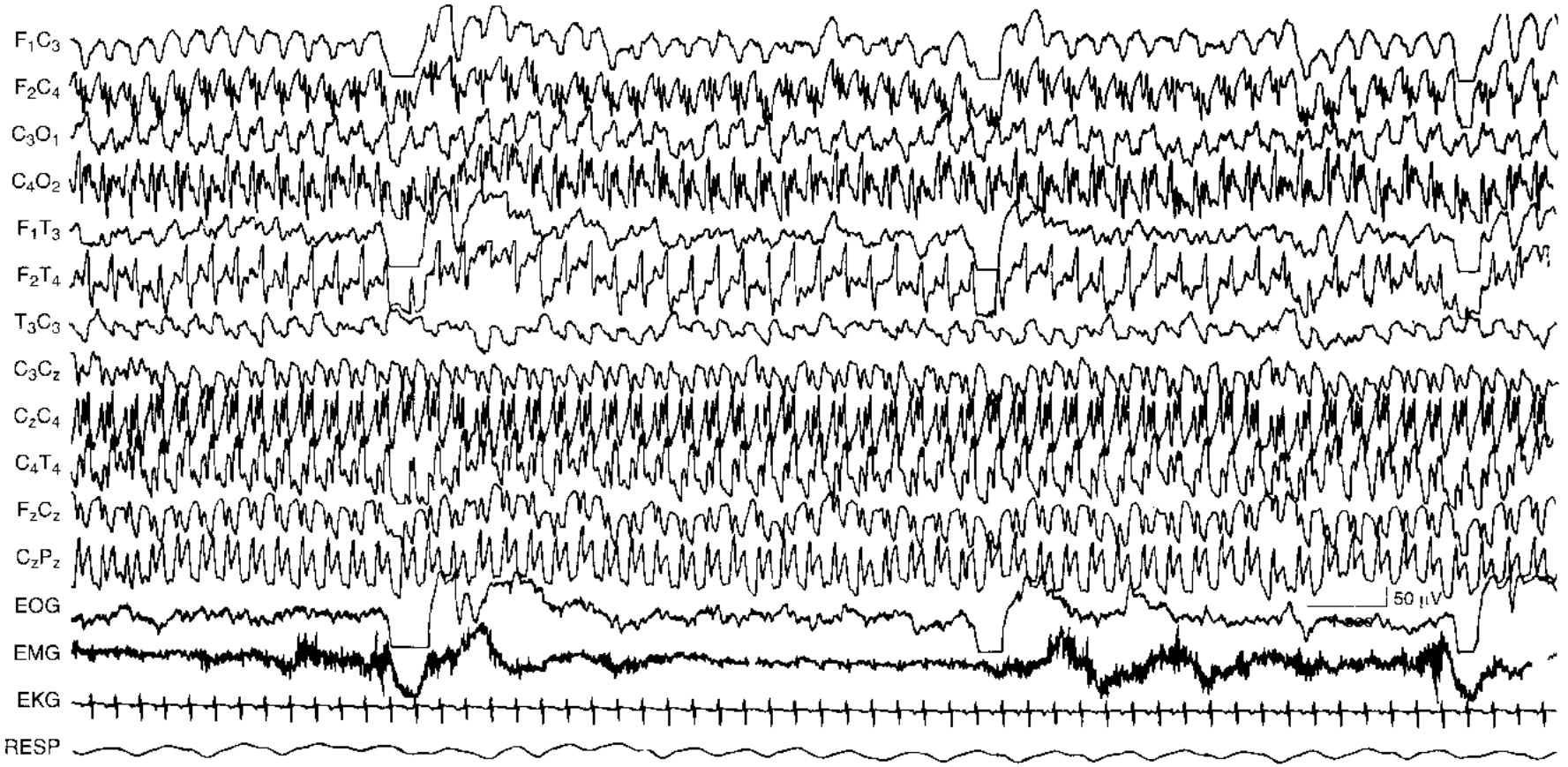


Figure 7.19 Complex morphology of seizure discharges. There are right central-midline central seizure discharges characterized by rhythmic slow activity with superimposed waves of faster frequency. This activity is reflected at lower voltage on the left. There is also independent electrical seizure activity in the right temporal region, consisting of rhythmic sharp waves. This is associated with a clinical seizure characterized by focal clonic activity of the left arm and leg. The EEG background activity is within the range of normal variation (not shown). The EEG is from a 6-week old, 37-week gestational age (43-week CA) with a history of congenital renal dysplasia and renal failure, with eventual right frontal lobe infarction and a porencephalic cyst in that region.

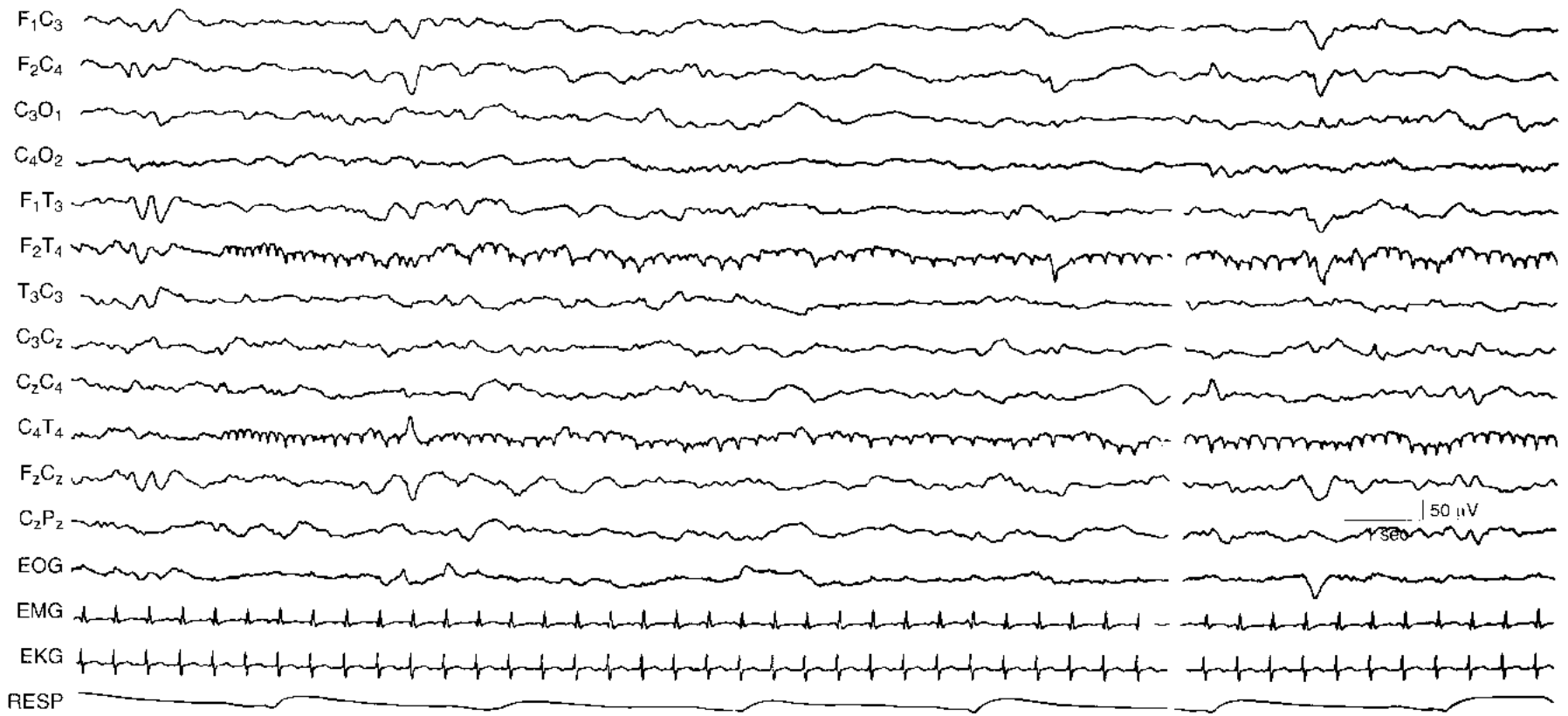


Figure 7.20 Highly localized electrical seizures. Low voltage, rhythmic, fast sharp waves arise in the right temporal region and remain confined to that region throughout the seizure. No clinical events were associated with the seizure discharge. The background EEG activity is depressed and undifferentiated (not shown). The EEG is from a 40-week CA infant with chronic hypoxemia due to congenital heart disease that included transposition of the great vessels treated with balloon atrial septostomy.

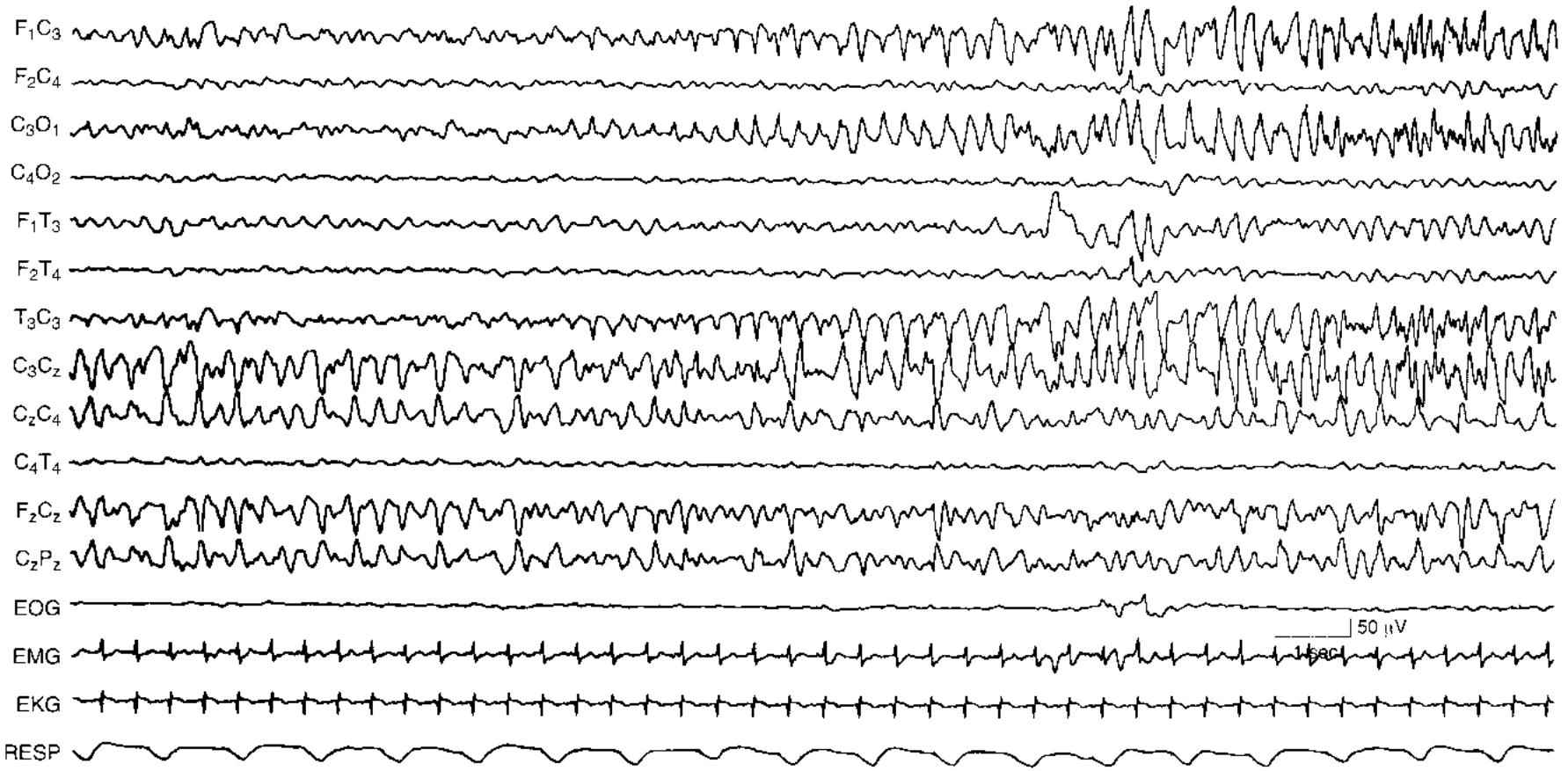


Figure 7.21 Spread of electrical seizure activity. Electrical seizure activity begins in the midline central region (Cz) then shifts to the left central region (C3) with less involvement at Cz. No clinical seizures were associated with the electrical seizure. The background EEG activity was characterized as suppression burst (not shown). This EEG is from a 40-week CA infant with hypoxic-ischemic encephalopathy, persistent pulmonary hypertension, hepatic failure, and disseminated intravascular coagulation.

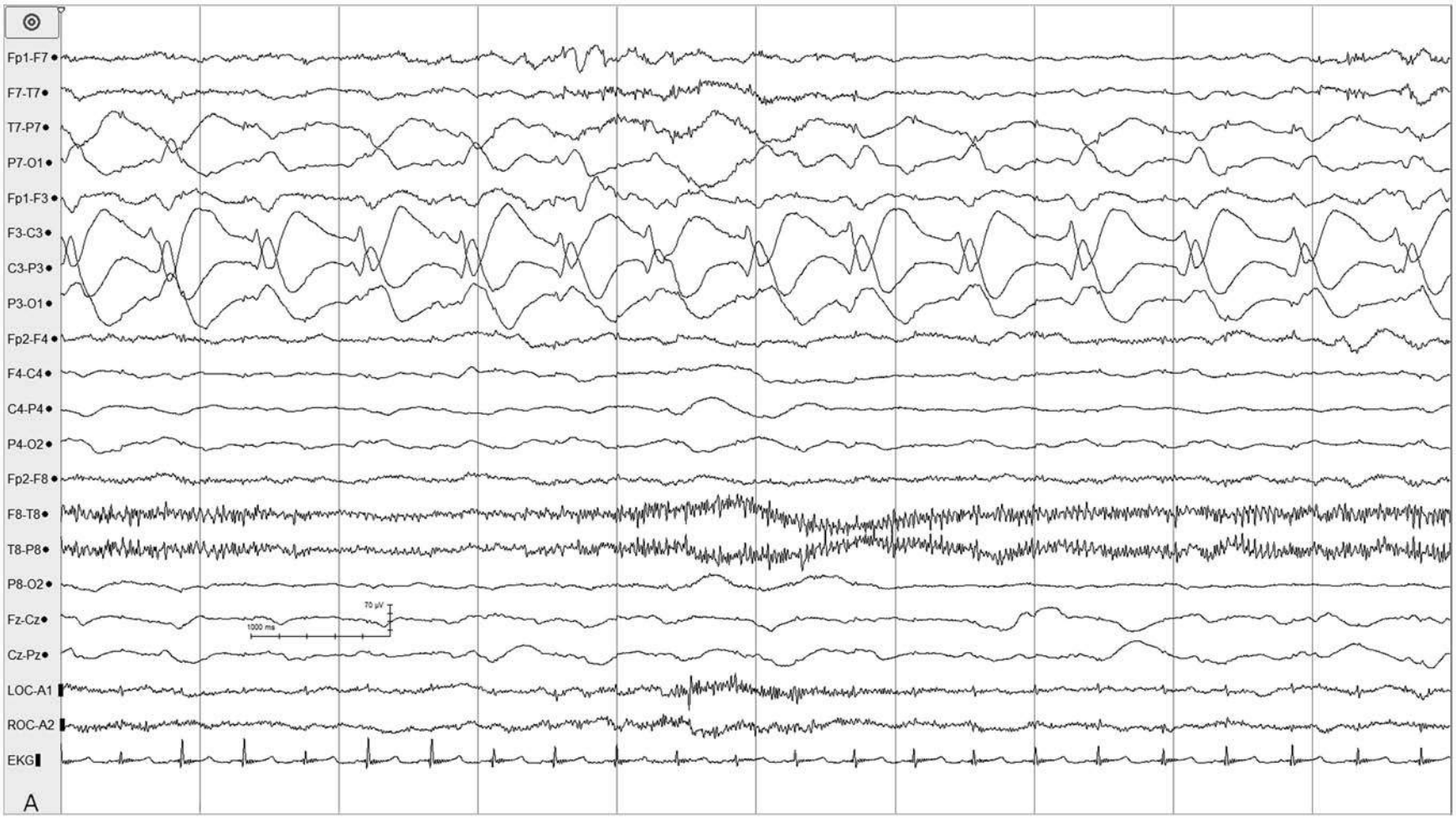


Figure 7.22 (A)–(F) Independent simultaneous onset of electrographic seizure activity. (A) Electrical seizure activity begins in the left central region as rhythmic slow sharp and slow wave activity. (*continued*)

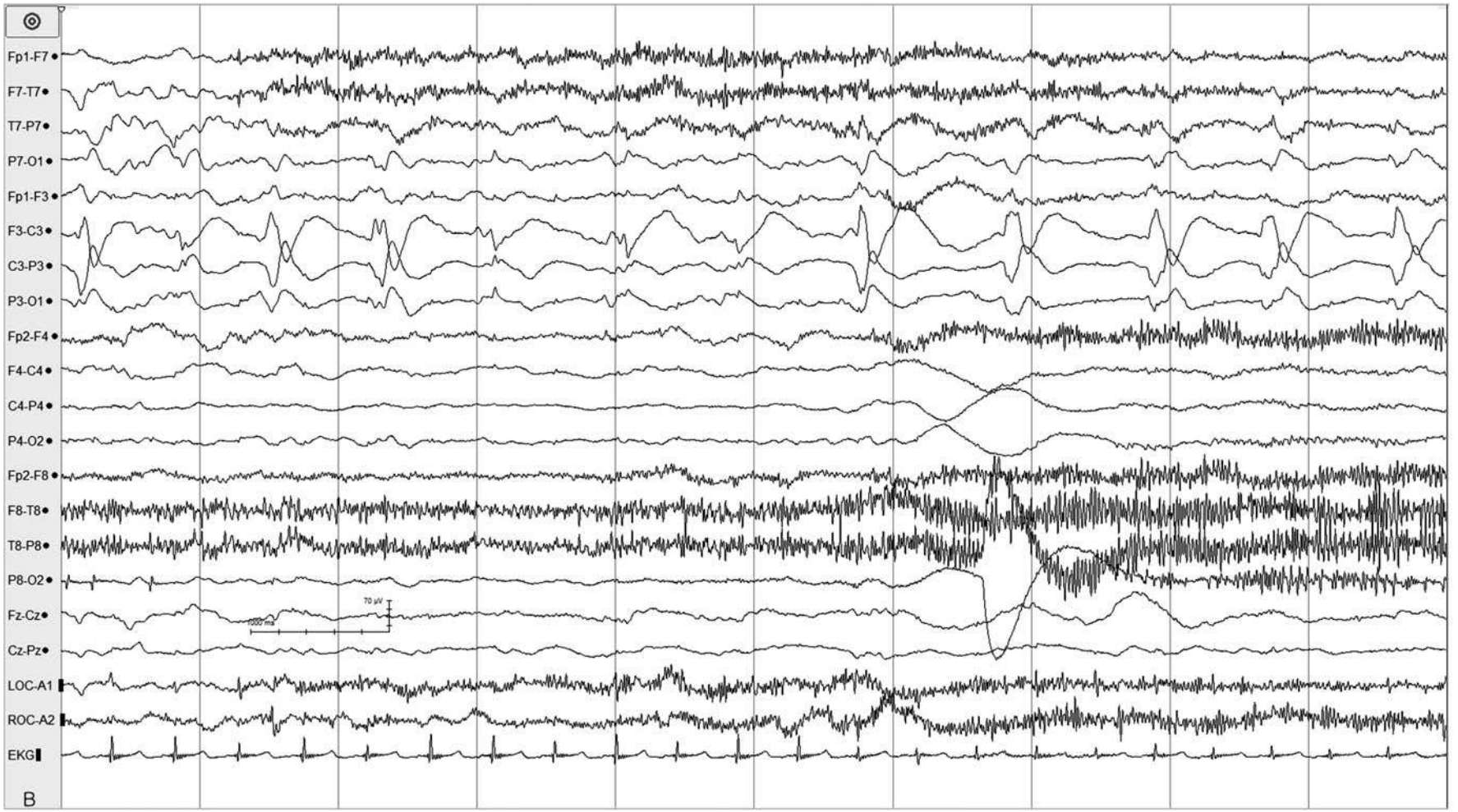


Figure 7.22 (*continued*) **(B)** 40 seconds later, it still remains confined to that region with some changing morphology. (*continued*)

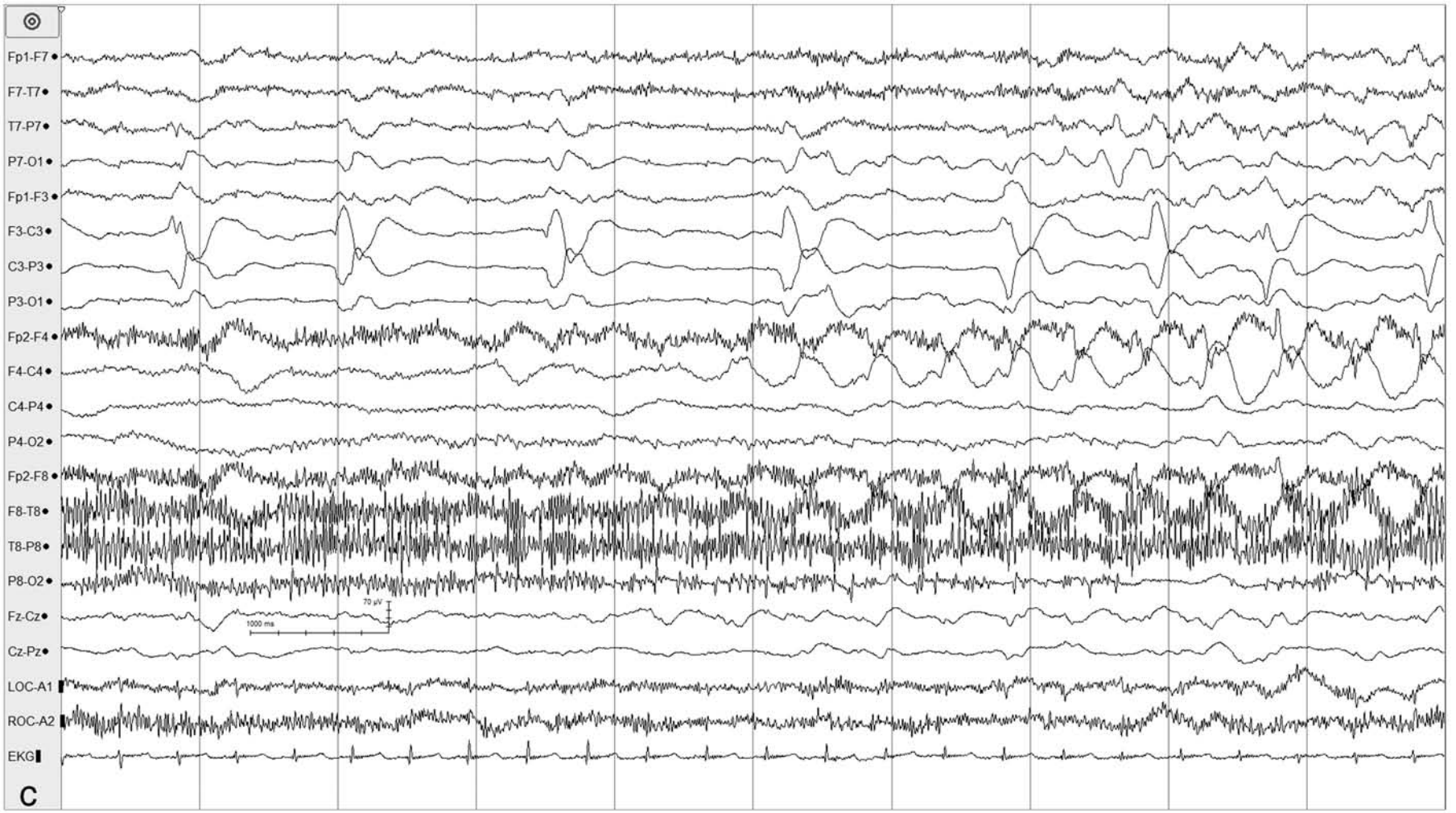


Figure 7.22 (*continued*) **(C)** 10 seconds later, an independent electrical discharge arises in the right frontal region initially with a slow wave morphology, while the discharge in the left central region persists at a slowed rate. This may appear as spread of discharge, but may also be interpreted as the onset of a simultaneous, but independent, discharge. (*continued*)

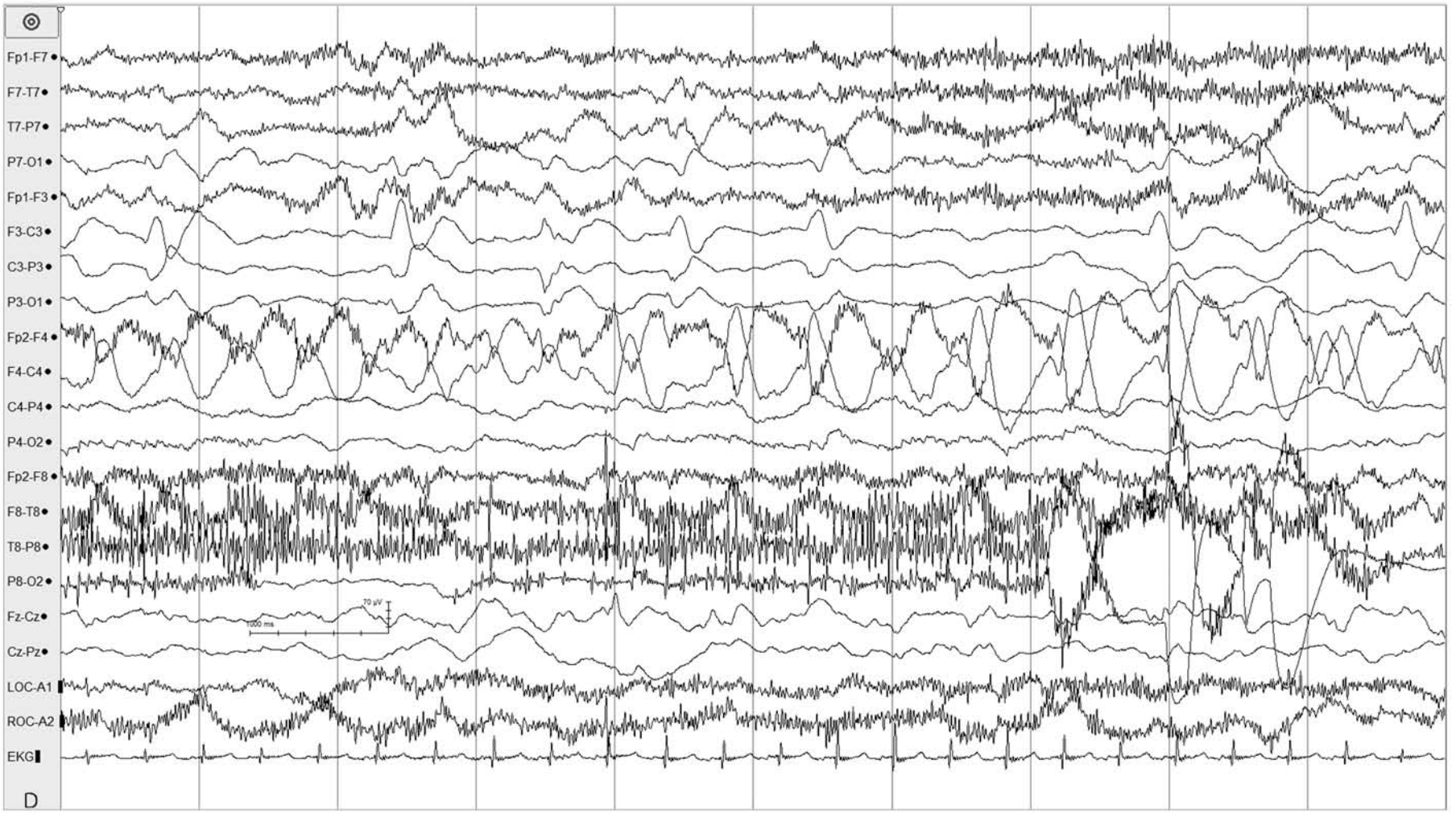


Figure 7.22 (*continued*) **(D)** 10 seconds later, the right frontal discharge persists as the left central discharge subsides. (*continued*)

Figure 7.22 (*continued*) **(E)** 40 seconds later only the right frontal discharge persists with a changing morphology consisting of sharp and slow waves. (*continued*)

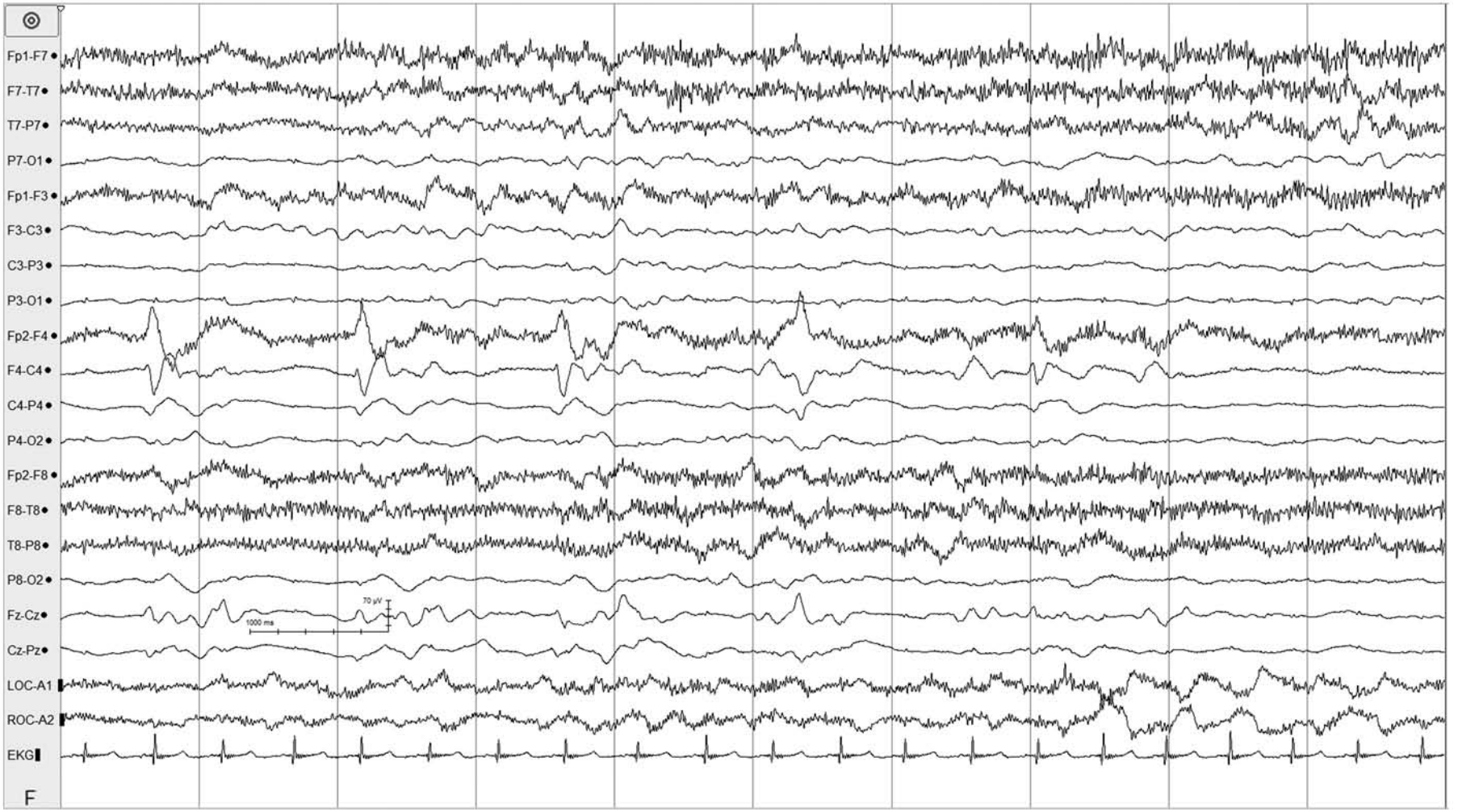


Figure 7.22 (*continued*) **(F)** After another 40 seconds, the right frontal discharge resolves. The duration of the electrographic seizure from left central onset to right frontal resolution was approximately 140 seconds. This occurred in an infant born at 34 weeks gestational age and recorded at 41 weeks CA and with cerebellar hypoplasis, dysplasia of the corpus callosum, simplified gyral pattern, and grey matter heterotopias. The background activity is low in voltage and undifferentiated.

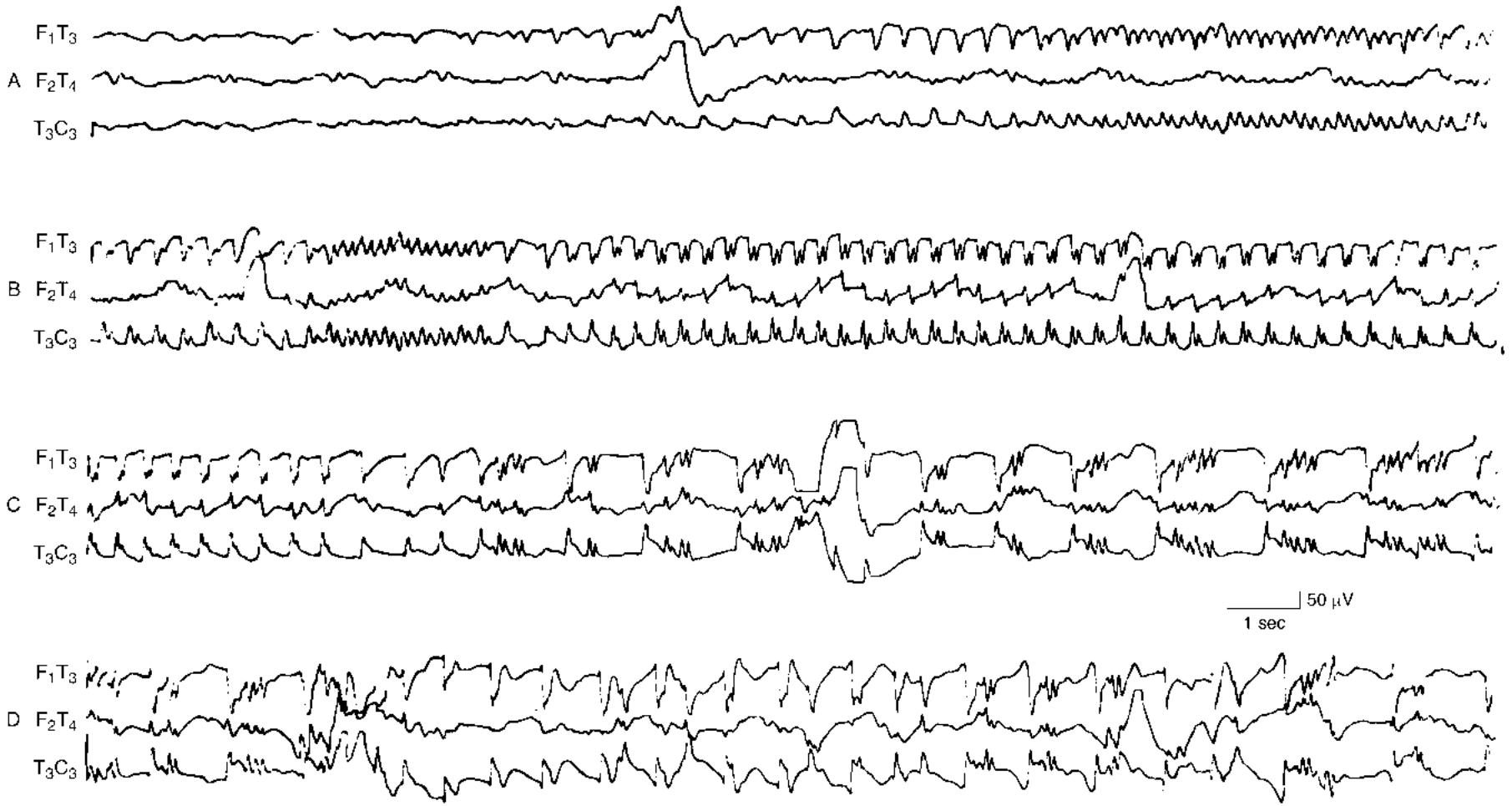


Figure 7.23 (A)–(H) Evolution in appearance of a single electrical seizure. (A)–(D) These samples of three selected channels of a 12-channel EEG show a single electrical seizure from beginning to end. The seizure is confined to the left temporal region with a changing morphology of the waveforms. No clinical seizures were associated with these electrical seizures. The background activity is depressed and undifferentiated (not shown). This EEG is from a 40-week CA infant with meconium aspiration, hepatic and liver failure, hypoglycemia, and hypoxic-ischemic encephalopathy. (*continued*)

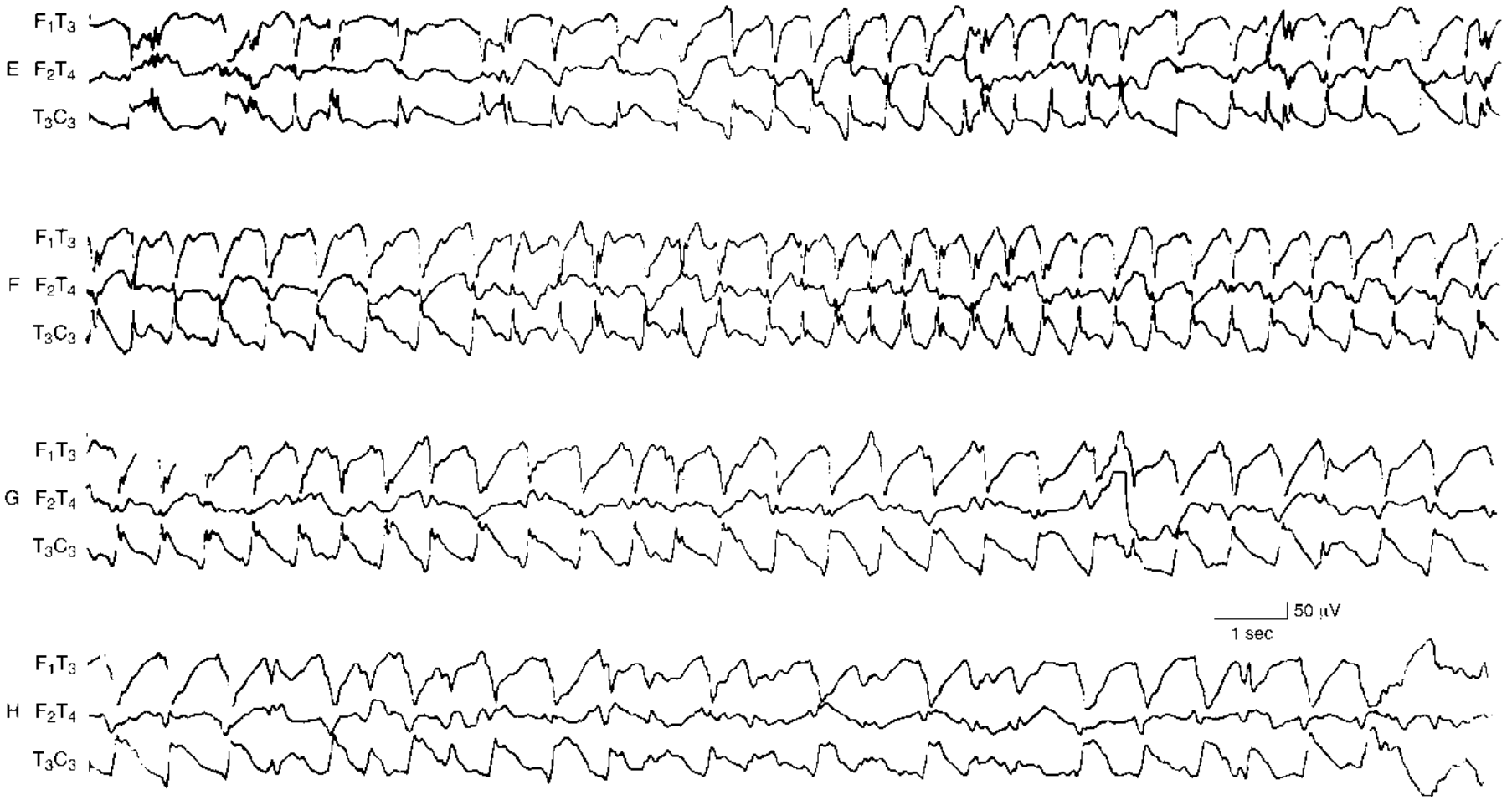


Figure 7.23 (*continued*)

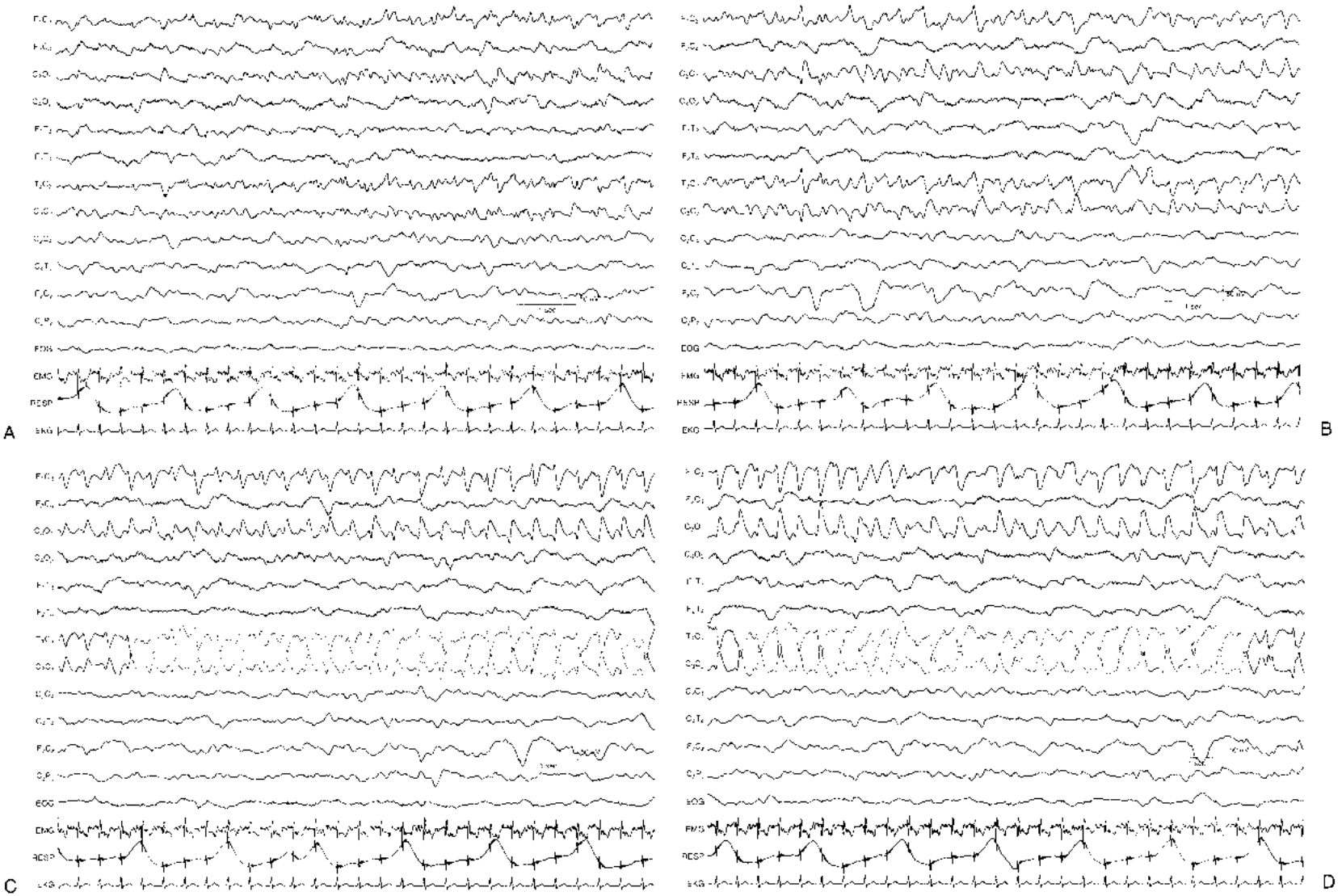


Figure 7.24 (A)–(H) Evolution in appearance of a single electrical seizure. (A)–(D) One electrical seizure that lasts approximately 80 seconds is shown in eight contiguous samples. The seizure begins as low voltage rhythmic theta activity in the left central region. There is a change in frequency and morphology throughout the seizure with its termination as slowly repetitive periodic transients. The background EEG activity is undifferentiated (not shown). This EEG is from a 3-week-old infant, born at 40-weeks gestational age (43-weeks CA) with pyloric stenosis, intractable vomiting, and multiple electrolyte metabolic disorders. (*continued*)

Figure 7.24 (*continued*) **(E–H)**

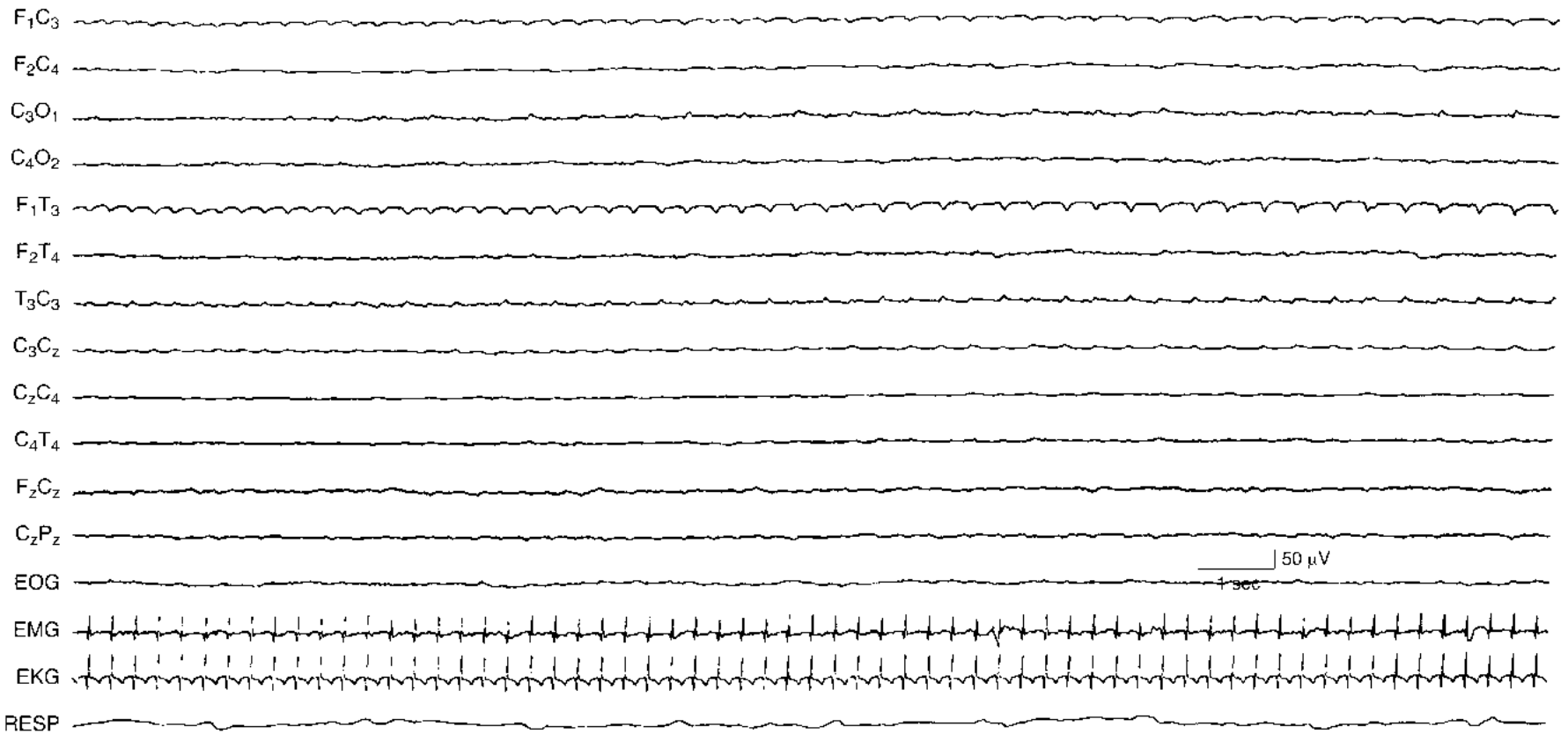


Figure 7.25 Seizure discharge of the depressed brain. There are low voltage, rhythmic, monomorphic, slow sharp waves in the left temporal region that persist virtually unchanged during the recorded seizure. No clinical seizures occurred during the electrical seizure. The background EEG is depressed and undifferentiated. This EEG is from a 38-week CA infant with persistently low APGAR scores, acidosis, subsequent multisystem organ failure, and hypoxic-ischemic encephalopathy.

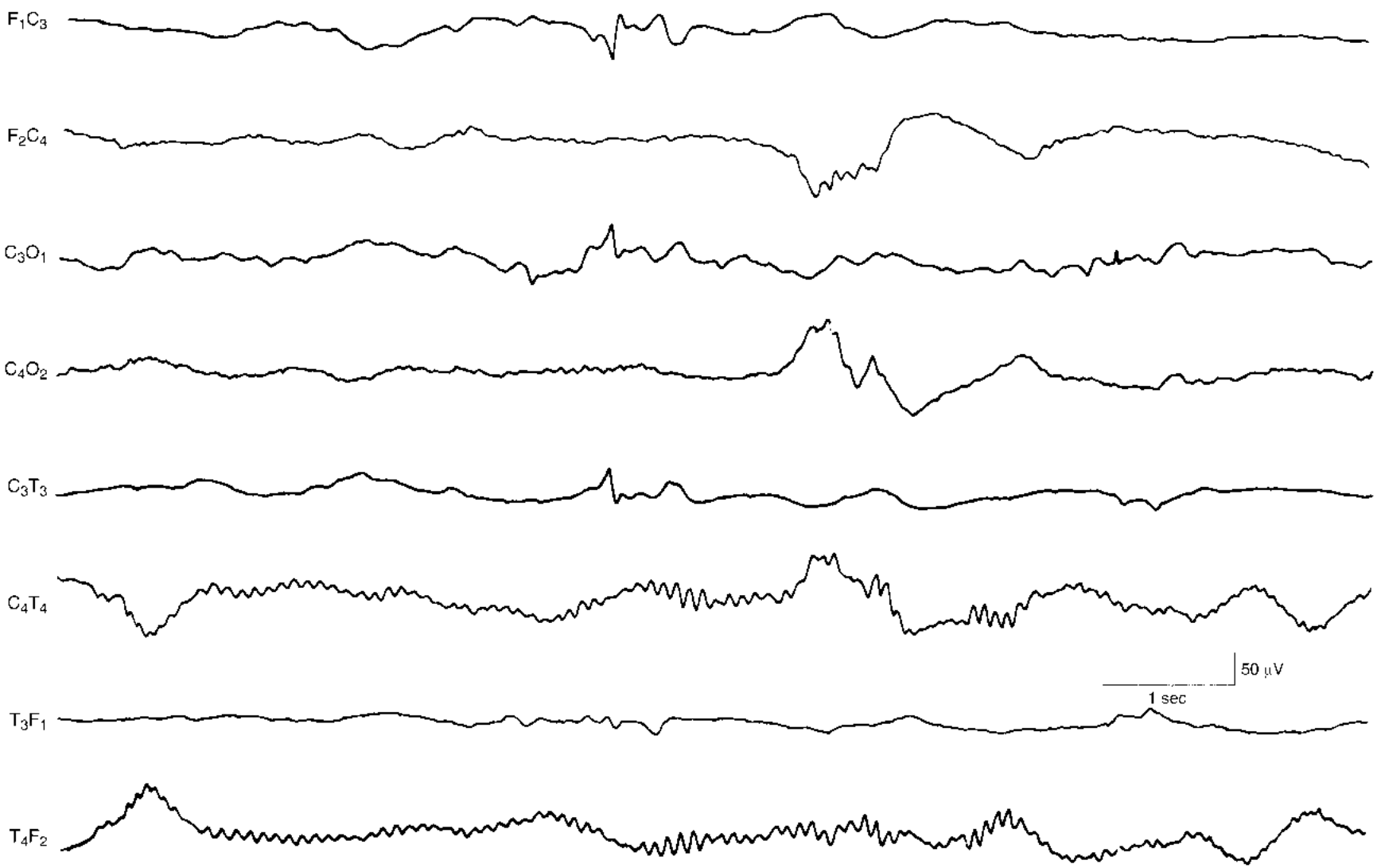


Figure 7.26 Alpha seizure discharge. An alpha seizure discharge arises abruptly from the right temporal region, characterized by rhythmic sinusoidal activity. No clinical seizures were associated with this electrical seizure. The background activity is depressed and undifferentiated (not shown). This EEG is from a term infant with hypoxic-ischemic encephalopathy.

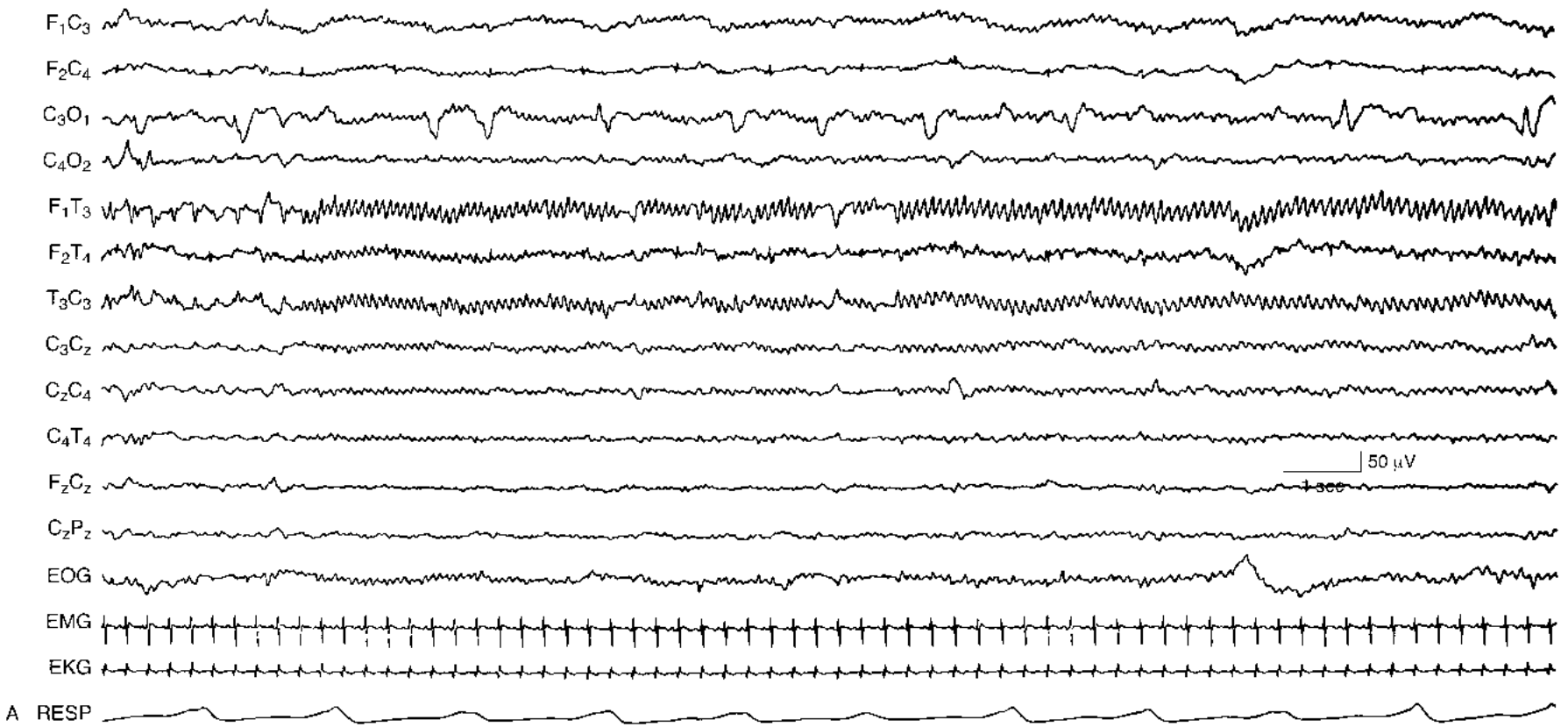


Figure 7.27 (A) and (B) Modulation of an alpha seizure discharge. (A) A seizure discharge is present in the left temporal region characterized by sinusoidal 10 to 11 Hz rhythmic activity that evolved from rhythmic sharp wave activity. There are also independent, semiperiodic slow wave transients in the left occipital region. This EEG is from a 38-week CA infant with pneumococcal meningitis. (*continued*)

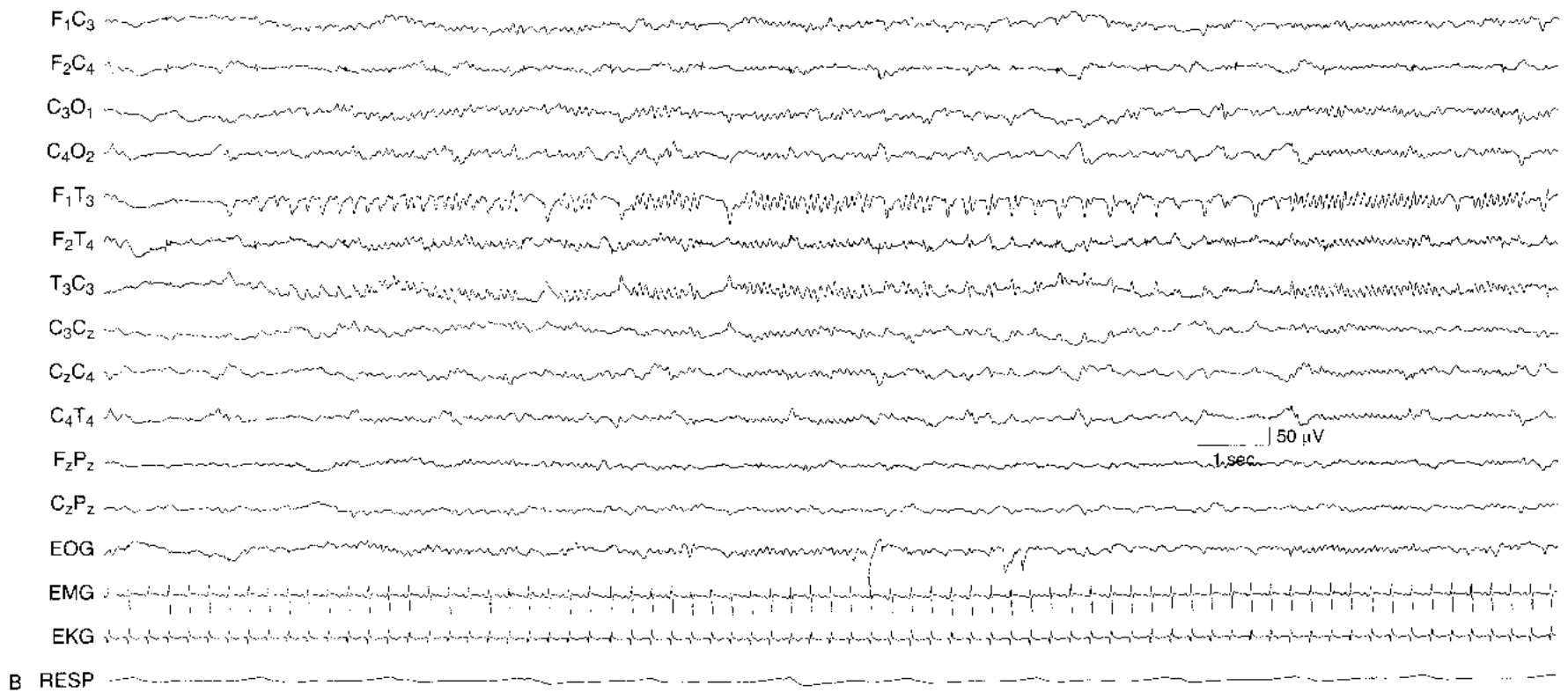


Figure 7.27 (*continued*) **(B)** Later in the same recording the electrical seizure modulated abruptly. No clinical seizures occurred during these electrical seizures. The background activity is depressed and undifferentiated.

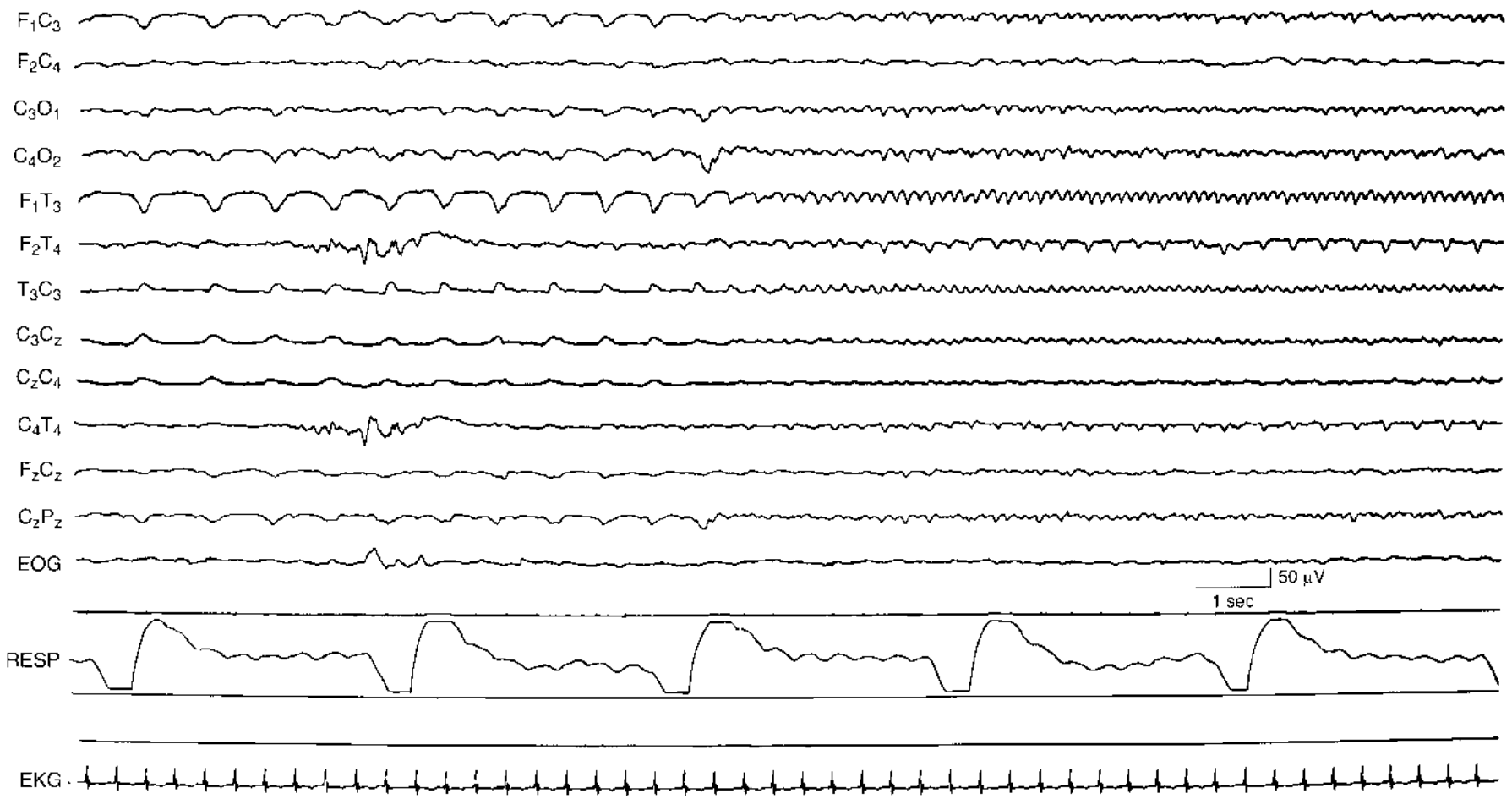


Figure 7.28 Alpha seizure discharge coexisting with another seizure discharge. A seizure discharge characterized by rhythmic 8 Hz sinusoidal activity evolves from rhythmic, slow, sharp wave activity in the left frontal temporal region. Approximately halfway through this segment of EEG, an independent seizure discharge arises in the right temporal region consisting of low voltage, rhythmic, slow, monomorphic sharp waves that can be characterized as seizure discharges of the depressed brain. No clinical seizures accompanied these electrical seizures. The background EEG activity is depressed and undifferentiated (not shown). This EEG is from a 12-week-old, former 26-week gestational age (38-week CA) infant who was initially hospitalized through the first 10 weeks of life then discharged. He was readmitted 2 weeks later with non-accidental head trauma with CT demonstrated diffuse and bilateral cerebral edema; focal parenchymal hemorrhages in the left temporal, parietal, and occipital lobes; and posterior fossa subarachnoid hemorrhage.

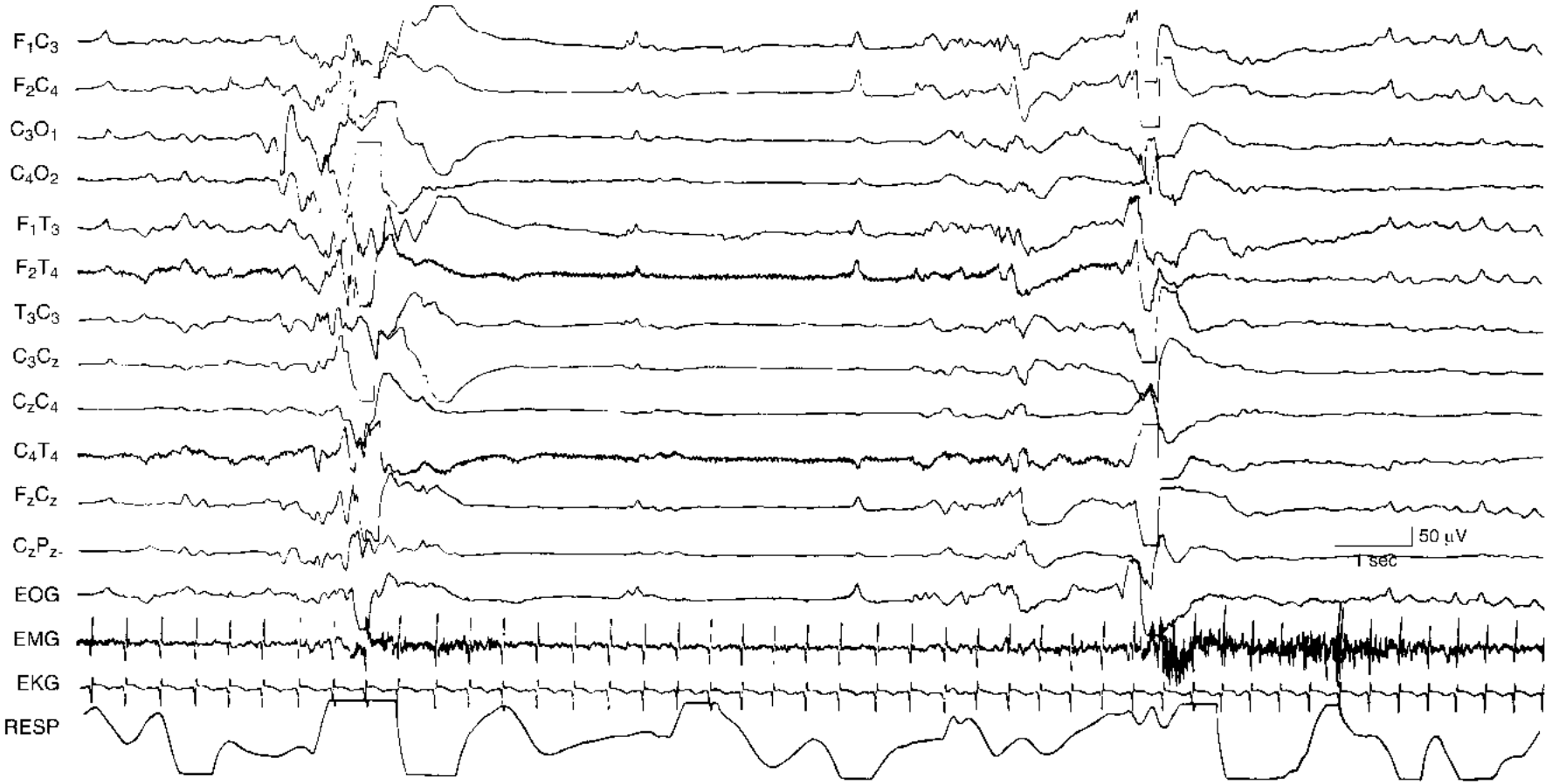


Figure 7.29 Seizure discharges with generalized myoclonus. Moderately high voltage generalized transients are associated with myoclonic seizures characterized by brief, axial movements involving the trunk and shoulders. The background activity is characterized by a suppression-burst pattern. This EEG is from a 36-week CA infant with lissencephaly.

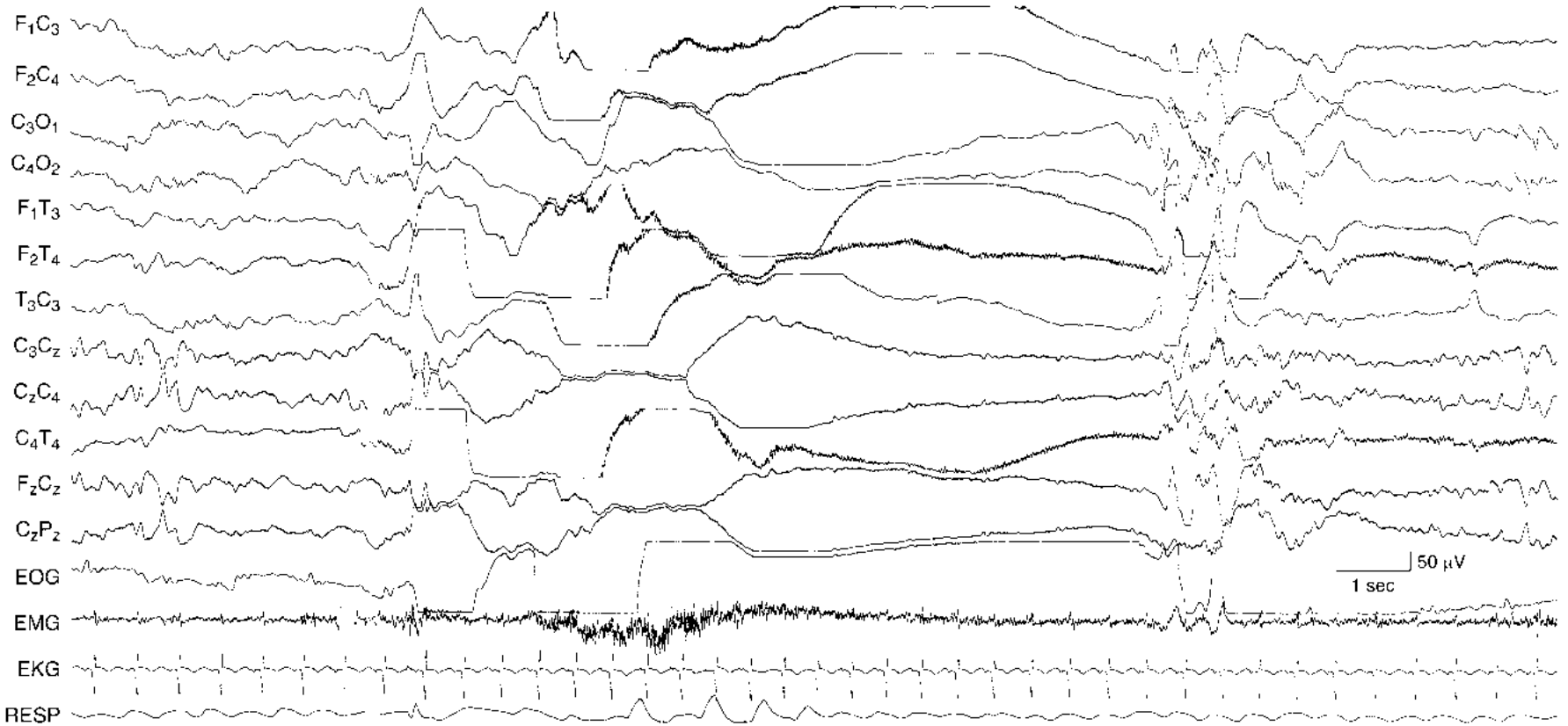


Figure 7.30 Generalized voltage attenuation with a spasm. This infant experienced a generalized flexor spasm associated with a generalized voltage attenuation. This EEG is from a 39-week CA infant with meconium aspiration, persistent pulmonary hypertension and hypoxic-ischemic encephalopathy.

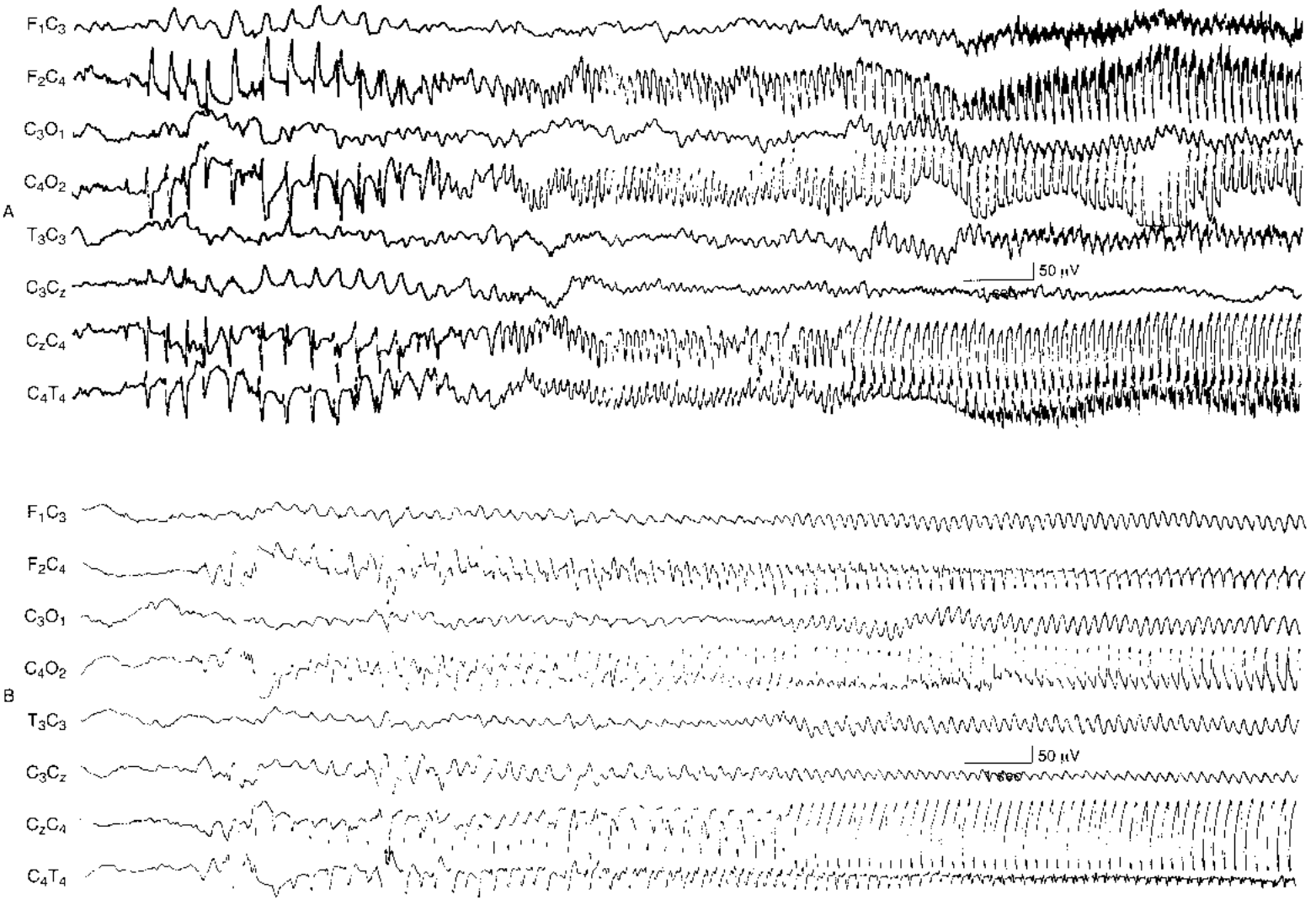


Figure 7.31 (A) and (B) Response to acute antiepileptic drug therapy. (A) Electrical seizure activity arises from the right central region and clinically is associated with a focal clonic seizure of the left arm. This sample of the EEG is recorded prior to AED therapy. **(B)** The infant then received phenobarbital (loading dose, 20 mg/kg IV) and experienced no further clinical seizures. However, later, during continued EEG recording there was a recurrence of the electrical seizure activity in the same region as before AED therapy. No clinical seizures occurred during this electrical seizure. This is considered a "decoupling" of the clinical seizures from the electrical seizures. This EEG is from a 40-week CA infant with a region of focal cortical dysplasia in the right parietal lobe near the midline (Hrachovy et al., 1990, with permission).

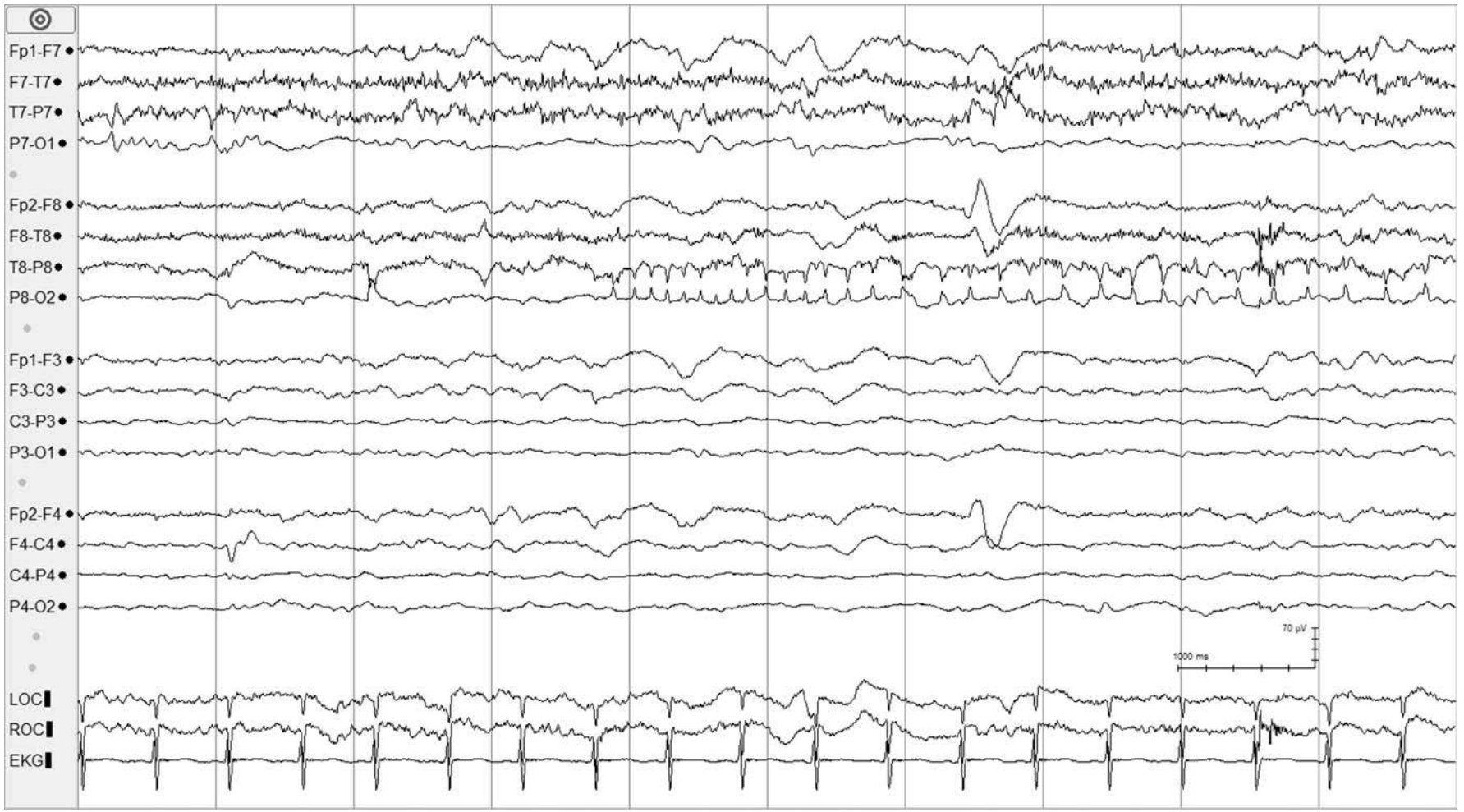


Figure 7.32 Electrical seizure emerging during hypothermia protocol. During Day 3 of hypothermia protocol, electrical seizure activity emerges in the right parietal region (temperature 90.1°F, 32.3°C) (same recording as Figure 6.10).

References

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